Neurology

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1. Sainz, A.: To be published. 2. Noce, R. H., Williams, D.B., and Rapaport, W.: In press. 3. Kline, N.S.: Ann. New York Acad. Sc. *59*:107 (April 30) 1954. 4. Catlett, J.M., and Gunn, C.G.: To be published.

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NEUROLOGY is published monthly at 84 South Tenth Street, Minneapolis 3, Minnesota, by LANCET PUBLICATIONS, INC. Subscription rate: $12.00 a year, $1.00 a copy; outside U.S. $13.00 a year, $1.10 a copy. Entered as second class matter at the postoffice at Minneapolis, Jan. 23, 1951.

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Volume 4, Number 12

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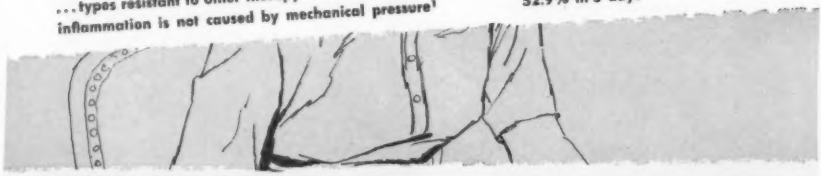

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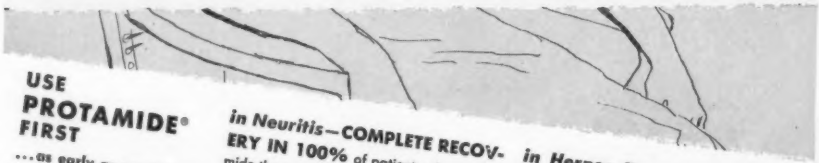

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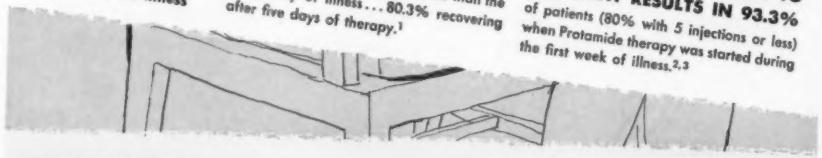

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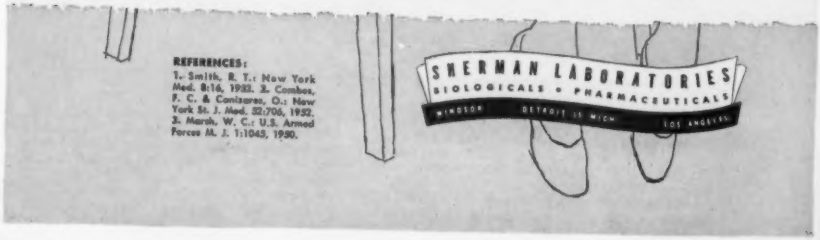

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INFORMATION FOR *Authors*

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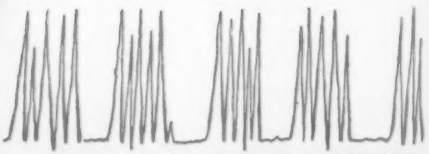

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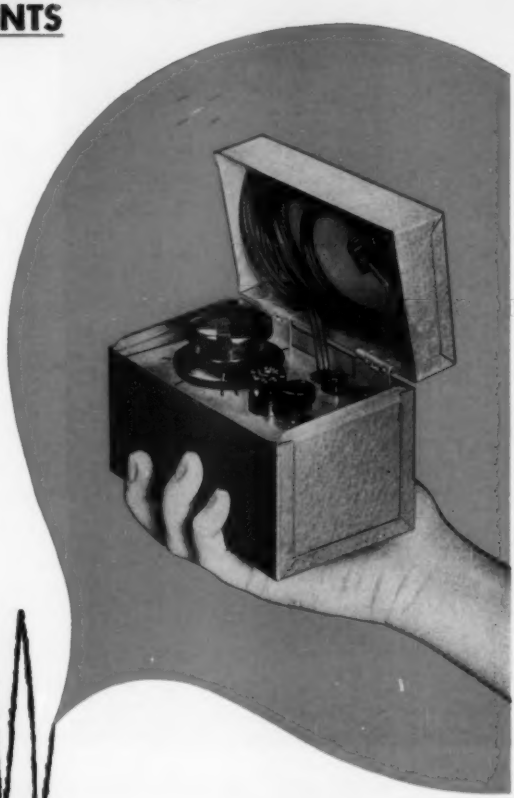

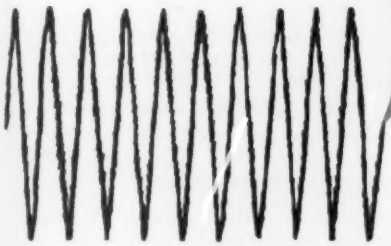

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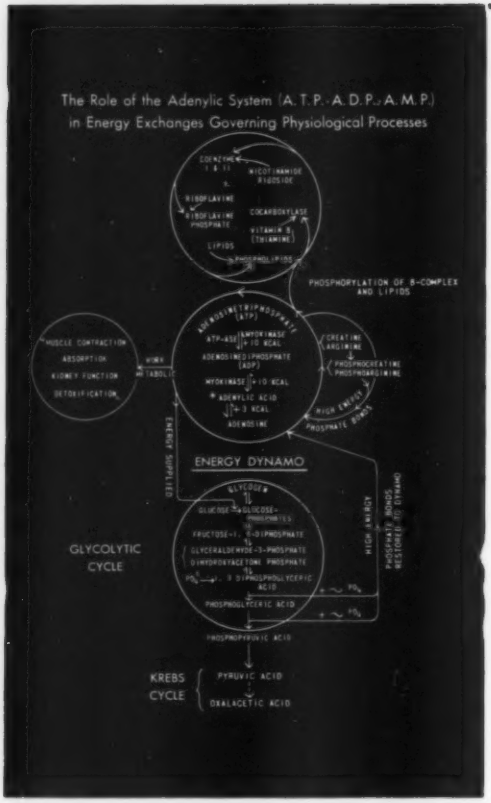
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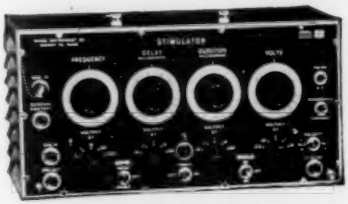

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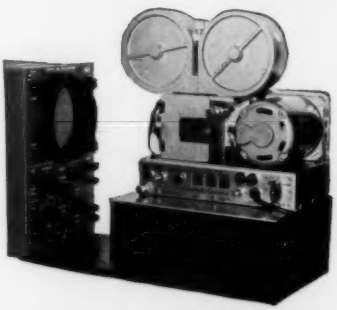

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Neurology

Spinal Cord Dysfunction from Cervical Intervertebral Disk Disease

W. Eugene Stern, M.D. and Robert W. Rand, M.D.

CERVICAL SPINAL CORD COMPRESSION is quite variable in its clinical manifestations, and cervical intervertebral disk disease as a cause of cord compression is no exception. The syndromes of unilateral cervical radiculitis resulting from annular protrusion and nuclear extrusion from the intervertebral disk have received generalized recognition and acceptance and need little emphasis. Well recognized also is the syndrome of combined unilateral radiculitis and cord compression. The radix which is involved assists in accurate clinical localization of the site of compression. In the case of midline cervical cord compression from intervertebral disk disease, however, the story is different. The localizing values of radiculitis are missing, and recognition of the location of the disease process, not to mention its nature, is frequently difficult. It is worth noting that although examples of midline protrusion with cord compression simulating neoplasm (ecchondromas) were among the earliest recognized forms of cervical intervertebral disk pathology responsible for neurologic disease, yet it is this very process which still taxes the clinical acumen of the neurologist. If we but note the combination of the disease process and its unique location we may surmise the problems present in diagnosis.

We would invite attention to five clinical case studies.

CASE MATERIAL

Case 1.—A 46 year old Negro male bootblack was admitted to the hospital September 15, 1952.

From the division of neurologic surgery, department of surgery, University of California Medical Center, Los Angeles, and the section of neurologic surgery, Veterans Administration Center, Los Angeles.

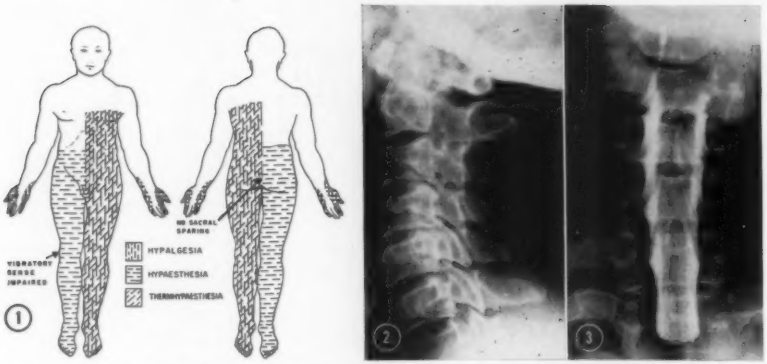


FIG. 1. Sensory chart demonstrating a Brown-Séquard pattern of loss, together with sparing of the right upper body quadrant. Note cervical dermatome involvement above the site of trunk sparing.

FIG. 2. Lateral cervical spine roentgenogram showing slight loss of interspace between C4 and C5.

FIG. 3. Myelographic study. Note the incomplete block opposite the body of C5.

Present illness. In May 1952 the patient had noticed a sense of heaviness and weakness in his right lower extremity followed by numbness in both hands and awkwardness in their use, together with numbness in the arms, legs, and trunk. At the same time he was aware of pain in the posterior cervical region, in the midscapular area, and along the posterior aspect of his right thigh. By June 1952 spasms in the right hip and in the muscles of the right arm occurred. Weakness and disability of gait increased in severity, and two weeks before admission he noted difficulty in initiating his urinary stream. There was no history of injury.

Examination. Examination revealed tenderness over the spinous processes of C3 through C7; extension of the cervical spine caused shooting pains across the lateral aspect of both arms to the elbows. There was moderate weakness in both upper and lower extremities, the right side being more involved than the left. The patient walked with a shuffling gait. Tone was increased in the extremities, more on the right than on the left, particularly in the extensor musculature of the lower extremities. The right thenar muscles were sore to touch. Both proximal and distal muscles of the upper extremities were weak. No atrophy was noted. The left biceps and triceps reflexes were less brisk than the right. The muscle-stretch reflexes were increased in the lower extremities. The abdominal reflexes were present in all four quadrants, the plantar responses were extensor on the right and equivocal on the left, and a positive Hoffmann response was obtained on the right side. The sensory impairment is demonstrated in the accompanying chart (figure 1).

Lumbar cerebrospinal fluid studies demonstrated the presence of a complete manometric block and a total protein of 67 mg. per cent. Cerebrospinal fluid and blood serologies were negative. Roentgenograms of the cervical spine revealed some loss of interspace between C4 and C5 (figure 2). Cervical myelography demonstrated an incomplete block centrally in the canal opposite the body of C5, with a trickle of opaque material in the right gutter (figure 3). Cervical laminectomy of C4, C5, and C6 was performed on September 23, 1952. The cervical spinal cord was displaced posteriorly in its midportion, and after release of ligaments an extruded piece of intervertebral disk nuclear material was removed at the C4-5 level transdurally. This material obviously had compressed the cord from the midline anteriorly. One year postoperatively the patient demonstrated marked improvement in balance and strength of extremities and disappearance of paresthesias in association with neck movements.

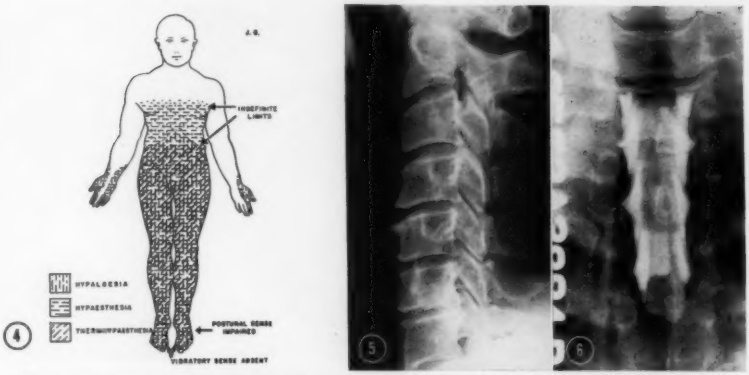


FIG. 4. Sensory chart demonstrating the unusual upper extremity involvement, the dissociation between pain and temperature in the upper trunk, and the vague limits to the deficit.

FIG. 5. Lateral cervical spine roentgenogram showing a straight spine, lipping of the body of C5, and loss of interspace between C6 and C7.

FIG. 6. Myelographic study showing the block at the C6-7 juncture.

Case 2.—A 42 year old white male kitchen helper was admitted to the hospital August 12, 1953.

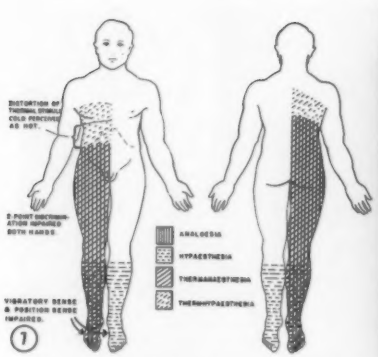
Present illness. In August 1952 the patient noticed burning, painful cramps in the muscles of his right lower extremity, particularly in the region of the thigh. Within four days he noted weakness in one of his lower extremities. Within 48 hours of the onset of weakness on one side, he experienced weakness in both lower extremities and fell on two occasions. He was aware of weakness in his left upper extremity associated with a burning sensation, together with a sharp pain running from the left shoulder along the mesial aspect of the arm to the wrist. The weakness increased in severity over a period of two weeks, remained static for two weeks, and then gradually improved thereafter until June 1953. During this illness an elevated spinal fluid protein led to the diagnosis of Guillain-Barré syndrome.

Strength was all but normal by June 1953, at which time gradual fatigue and weakness again developed in the same three extremities over a period of two weeks. Fleeting occurrences of pain in the left upper extremity also returned. He noted band-like sensations about his abdomen and a sensation of numbness over his entire body.

Past history revealed an injury in 1947 when he rolled over in an automobile and was amnesic for an unknown period of time.

Examination. A mild degree of nuchal guarding and stiffness together with limitation of neck movements were noted. There was weakness and increased tone in the left upper extremity and both lower extremities. The patient walked with a stiff, cautious gait. Reflexes in the left upper extremity were increased compared to the right side. The reflexes were increased in both lower extremities. The right lower abdominal reflex only was found, and the plantar responses were extensor bilaterally. The impaired sensation is presented in figure 4. Lumbar cerebrospinal fluid porteins on two occasions were 96 and 124 mg. per cent. Roentgenograms of the cervical spine revealed degenerative intervertebral disk disease with loss of interspace at the C6-7 level. Lipping of the body of C5 and straightening of the entire cervical column were seen (figure 5). Cervical myelography demonstrated a filling defect opposite the C6-7 junction (figure 6).

Cervical laminectomy on October 12, 1953 disclosed a normal appearing midcervical spinal cord. After release of the dentate ligaments, rotation of the cord exposed a promi-



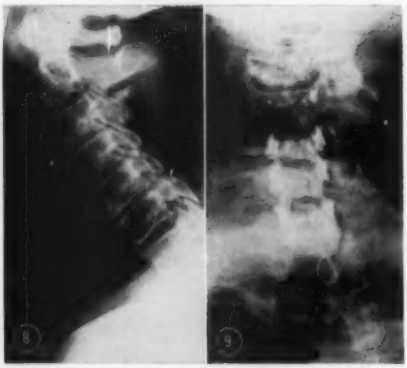


FIG. 7. Sensory chart showing the sharply dissociated pattern limited to the right side of the body. Note the area of perversion of thermal stimuli on the trunk.

FIG. 8. Postoperative lateral roentgenogram demonstrating the metallic marker opposite the C5-6 interspace, at which level degenerative disease can be seen. Milder changes can be seen at the C3-4 level.

FIG. 9. Mylographic study which outlines a block at the C4-5 level. The offending protrusion was encountered at the next lower interspace. This discrepancy is unexplained.

nent posterior bulge of what appeared to be a midline disk protrusion corresponding to the myelographic defect at the junction of the bodies of C6 and C7. A small bit of intervertebral disk material was removed transdurally.

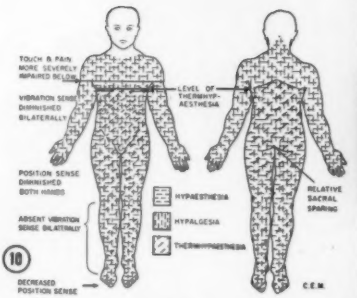
Disappearance of the extensor-plantar responses and of the sensory deficit were the major changes in the patient's status after his operative procedure.

Case 3.—A 59 year old unemployed Negro male diabetic was admitted to the hospital September 2, 1953.

Present illness. In 1950 the patient suffered rather abrupt onset of weakness in the left extremities. At the same time or shortly thereafter he noted numbness of his right lower extremity. Some improvement took place over the succeeding year, but in June 1951 weakness of the left side and numbness of the right side increased in severity. During the year before admission, the patient was aware of some progressive weakness in the right lower extremity. He noted progressive weakness in his abdominal muscles and complained of being unable to sit up in bed. This patient, a known diabetic, had an elevated blood pressure in 1938 and 1951. The only history of injury was an instance of fractured ribs which occurred in an automobile accident in 1946.

Examination. This revealed a man who was committed to the use of wheel chair and crutches. Fundiscopic examination demonstrated patches of exudate and tortuosity of the retinal arterioles. A mild bilateral ptosis was present. A subcutaneous lipoma measuring 6 cm. in diameter was located in the posterior cervical region. Neck mobility was not limited. There was a severe left hemiparesis with increase in tone and mild atrophy of the left biceps, triceps, and hamstring musculature. There were moderate to severe weakness and increase in tone in both lower extremities, less severe on the right side. There was definite atrophy of the interosseous musculature of the right hand without weakness. Muscle stretch reflexes were increased in the left upper extremity and in both lower extremities. The abdominal reflexes were absent and the plantar responses were extensor bilaterally. The very striking sensory deficit is recorded in the accompanying chart (figure 7).

Lumbar cerebrospinal fluid examination demonstrated normal manometric studies and a total protein of 54 mg. per cent. Serologies of the lumbar cerebrospinal fluid and blood were negative. Roentgenograms of the cervical spine revealed extensive degenerative joint



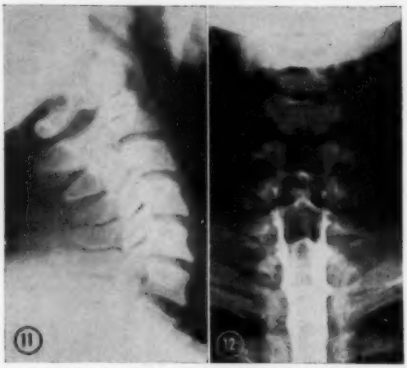


FIG. 10. Sensory chart showing the extraordinarily high sensory level, the dissociation between pain and temperature in the upper trunk, and the relative sacral sparing. Note that vibration sense was absent in both legs.

FIG. 11. Lateral cervical roentgenogram showing but slight narrowing and lipping at the C5-6 level.

FIG. 12. Myelographic study which demonstrates the apparent midline block to oil-flow at the C7-T1 level and the block to flow in the lateral gutters which becomes complete opposite the body of C6.

disease with hypertrophic spur formation. There was loss of interspace between the bodies of C5 and C6, together with spur formation and lipping (figure 8). Cervical myelography demonstrated an incomplete midline block opposite the juncture between C4 and C5 (figure 9).

Cervical laminectomy on October 26, 1953 showed the spinal cord itself to be normal, but one could see a rippling and undulation of the cord as it lay against the anterior surface of the vertebral canal. A midline intervertebral disk protrusion was noted opposite what we interpreted to be the C5-6 juncture; this was a firm protrusion and no attempt was made to excise any material transdurally. A silver clip was placed opposite this protrusion and corresponded in the postoperative film to the C5-6 juncture rather than to the site of incomplete block at the C4-5 juncture. The patient made an uneventful postoperative convalescence and was discharged from the hospital with no change in his neurologic deficit.

Case 4.—A 31 year old Negro male cotton picker was admitted to the hospital December 2, 1953.

Present illness. In August 1953 the patient noted onset of low back pain, with pain in both lower extremities. By September he suffered numbness in both upper extremities and shooting pains across both shoulders radiating into the arms and forearms. There was progressive weakness in both upper extremities, more marked on the right side. In October 1953 there were stiffness and progressive difficulty in the use of both lower extremities together with pain in the calves, and by December he noted numbness and tingling in his toes and some defect in initiating his urinary stream. In the past history there was a record of vascular hypertension but no history of injury to the head or neck.

Examination. The patient walked with an unsteady gait in a stiffened fashion, holding his neck in a guarded position. Neck mobility was limited. Extension of the neck and vertical compression of the cervical spine caused pain in the sacral region. Weakness in all four extremities was evidenced. In the upper extremities there were increase in tone of the extensor musculature of the elbow and atrophy of the intrinsic muscles of the hands. The patient had difficulty in performing fine finger movements. The muscle-stretch reflexes were increased in both upper and lower extremities with the exception of the right biceps response. The abdominal reflexes were absent; the plantar responses were bilaterally ex-

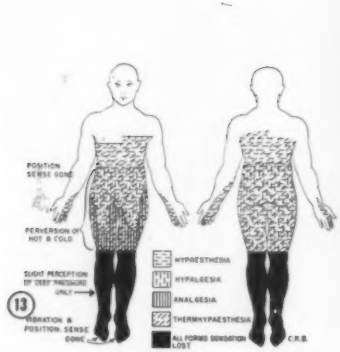


FIG. 13. Sensory chart showing the unusual upper extremity deficit, the dissociation between pain and temperature in the upper trunk, the perversion of thermal stimuli, and the unusually dense involvement to all forms of sensation in the lower extremities in a stocking pattern.

FIG. 14. Lateral cervical roentgenogram demonstrating slight narrowing and osteophyte formation at the C6-7 interspace. No fracture or dislocation was present.

FIG. 15. Lateral myelographic study showing the anteriorly oriented defect in the oil column at the C5-6 interspace. The slight defect at the C6-7 juncture does not show to good effect.

tensor. The sensory deficit is recorded in the accompanying chart (figure 10).

Lumbar puncture on January 15, 1954 showed a total protein of 126 mg. per cent, with evidence of an incomplete manometric block. Roentgenograms of the cervical spine demonstrated only slight narrowing between the C5-6 interspace with slight anterior and posterior arthritic lipping of the adjacent bodies of the vertebrae (figure 11). Myelography disclosed a midline arrest of the opaque oil opposite the interspace between C7 and T1. The opaque material flowed upward on either side of the midline in the lateral gutters to the level opposite the body of C6 (figure 12).

Cervical laminectomy on January 27, 1954 exposed a normal-appearing dura mater which did not pulsate until the lamina of C3 was excised. The cervical arachnoid was thickened and slightly hemorrhagic. At the level of C5 the spinal cord was displaced backward. As the dentate ligaments were released above and below the level of humping of the cord, namely between the C5 and C6 rootlets, the cord itself could be lifted aside to demonstrate the presence of a soft, bulging mass extending across the entire transverse width of the vertebral canal. By a transdural approach, pieces of extruded intervertebral nuclear material were removed from the C5-6 interspace.

The patient made an uneventful postoperative recovery and has evidenced a rapid disappearance of his sensory deficit and a marked improvement of his motor status.

Case 5.—A 41 year old white male epileptic was admitted to the hospital July 25, 1953.

Present illness. On July 16, 1953 the patient fell to the floor during a convulsive seizure and struck his forehead. Following a two-hour period of amnesia, he was unable to move either arms or legs. Within 24 hours he moved his arms but could not walk, and he noted increasing distension of his abdomen. Following a "spinal adjustment" he was admitted to the hospital nine days after injury.

Examination. The patient was in the early stages of acute alcoholic hallucinosis. The cervical spine was quite mobile and supple, but there was local tenderness over the spinous process of C5. Compression in this area caused sensations of electricity to pass into both hands and fingers as well as into the abdomen and thighs. With the exceptions of slight toe movements, both plantar flexion and dorsiflexion, there was no voluntary motor activity below the C5 level. The abdomen was distended, and peristalsis was diminished. The right

and left biceps reflexes were present. The triceps responses were absent on both sides. The brachioradialis reflexes were present but depressed on both sides. The patellar response was present on the right but absent on the left, and the Achilles reflex was present on the right but diminished on the left. The abdominal reflexes were absent and the plantar responses were extensor. The sensory deficit is recorded in the accompanying chart (figure 13).

Lumbar puncture and manometric studies demonstrated the presence of a complete manometric block. Roentgenograms of the cervical spine revealed slight narrowing of the interspace between C6 and C7 with osteophytes at this level. The normal cervical lordosis was absent, but no fracture or dislocation was present (figure 14). Cervical myelography demonstrated the presence of an incomplete midline myelographic block opposite the C5-6 juncture, with a slight additional bulge seen in the lateral projection opposite the C6-7 juncture (figure 15). A laminectomy on August 10, 1953 disclosed the spinal cord humped posteriorly at the level of the C5-6 juncture. No attempt was made to remove the midline disk until a second procedure one week later at which time several loose pieces of nuclear material of the C5-6 disk were excised. This resulted in a lessening of the angulation of the cord. Although disturbed by severe involuntary flexor spasms of the lower extremities postoperatively, the patient showed steady and continuous improvement in his strength. Interosseous atrophy developed in both hands within four weeks of injury.

COMMENT

The mode of onset varied in each of these five cases. Although remote injury may have caused the predisposition to intervertebral disk degeneration in cases 2 and 3, it was not easy to ascertain its relative importance in any but case 5 in which acute injury was responsible for the immediate and maximal cord damage, presumably from immediate acute disk protrusion. Constant complaints were paresthesias or pain, together with early weakness in the lower extremities.

In case 2 the dramatic remission between two subacute manifestations led to a consideration of a myeloradiculitis or a disseminated disease. Multiple sclerosis was a diagnosis entertained for case 4. In case 3 the striking unilateral dissociated sensory alteration decreed the diagnosis of intramedullary cord disease. Cervical cord and foramen magnum neoplasms and subacute combined disease were strongly considered in the clinical assessment of certain of our cases.

Of interest is a consideration of local cervical and upper extremity symptoms and signs. We are concerned with uncovering clues among these case studies which might point to the true location or nature of the disease. In case 1 the posterior cervical area was the site of pain at the onset of disease. Pain involved the base of the neck in case 4. Limited movement of the neck was admitted by two patients on direct questioning. In three cases, including case 5 with acute injury, there was tenderness along the posterior cervical spine. Extension of the neck in case 1 produced paresthesias into both upper extremities. The same maneuver in case 4 produced aggravation of sacral pain; palpation of the spine of the fifth cervical vertebra in case 5 (acute injury case) was responsible for electrical sensations passing into the hands, abdomen, thighs. Neck mobility was limited in three cases. It is noteworthy that the patient who had sustained an acute injury demonstrated no limita-

tion of cervical motions. A report of pain similar to radicular pain in one extremity was elicited from two patients (cases 2 and 4). Two patients suffered prominent but diffuse paresthesias in the hands and fingers. All but one patient demonstrated weakness in both upper extremities. Case 1 evidenced left upper extremity atrophy and weakness and right interosseous muscle atrophy without attendant loss of strength. Similar interosseous muscle atrophy was seen in case 4. The thenar muscles of case 1 were tender. Case 5 developed loss of interosseous substance bilaterally some weeks following his injury. In every case some differences in the upper extremity reflexes were noted upon comparing the two sides. However, such changes were not sufficiently discriminatory as to permit accurate localization within the cervical spinal cord.

The roentgenologic study of the cervical spine in these patients disclosed changes in the plain films in all cases, although the findings were only slight in case 4. The lumbar cerebrospinal fluid protein was elevated to 100 mg. or more in two cases. In one of these a manometric block was recorded, a finding present in two patients. Incomplete myelographic blocks with midline defects were present in all cases.

DISCUSSION OF SENSORY ALTERATIONS

Varying sensory patterns have been reported following extramedullary compression of the cervical spinal cord. Certain sensory patterns, whether clearly defined or only suggestive in degree, are recognized as signifying alternately intramedullary or extramedullary disease depending on the observer and the strength of his argument.

Dissociated patterns. Dissociation applies most often to pain and temperature sense on the one hand and tactile sensibility on the other. This dissociation existed in a hemicorporate pattern in case 3. Other forms of dissociation are also encountered: pain on the one hand and temperature sensibility on the other, dissociation between heat and cold, and vibration sense dissociated from position sense. The dissociation between pain and thermal sense was demonstrated in three of our cases. In cases 2 and 4 the thermhypesthesia stopped at a level many inches below the level for pain. In case 5 the reverse was true, that is, thermhypesthesia rose to a higher level than the deficit to pain.

Abrahamson and Grossman[1] noted this phenomenon from lateral compression of the cervical cord and commented upon the appearance of "intramedullary" signs late in the course of extramedullary compression. Tilney and Elsberg[2] observed so-called "syringomyelic dissociation" of sensation in extramedullary cervical cord tumors. It is significant that these authors found this tactile versus pain and temperature dissociation distinct in patients suffering compression of the ventral surface of the cord by an "extradural chondroma which had grown from the posterior surface of the body of the vertebra or the intervertebral cartilage." Elsberg and Strauss[3] recorded the late involvement of tactile sensibility, suggesting the similarity to intramedullary disease

when pain and temperature were involved early and touch was not involved until compression was advanced. Symonds and Meadows[4] confirmed this primary dissociation of touch and pain and called attention to the dissociation between vibratory and position sense, between thermal and other kinds of pain, and between heat and cold. These latter findings are well recognized as occurring in intramedullary cavitating disease,[5] but in every case reviewed by these authors they were due to extramedullary cervical cord compression.

The recent excellent accounts of cervical spondylosis presented by Brain and associates,[6] Spillane and Lloyd,[7] and Allen[8] understandably differ in the sensory alterations found among their cases. Spillane and Lloyd observed sensory changes among 12 of 21 cases, but in no case was dissociated anesthesia demonstrated. This was in contrast to the report of Allen who found crisp tract dissociation which might appear early and persist.

Sparing of large segments of the trunk with or without sacral sparing. This phenomenon was noted by Abrahamson and Grossman[1] and Tilney and Elsberg,[2] particularly in the caudal dermatomes from extramedullary compression of the midventral portion of the cervical cord. This escape of intermediate segments of the trunk and some dissociated trunk and sacral sparing were again emphasized by Symonds and Meadows.[4] Brain and associates[6] reported the occurrence of areas of trunk sparing and "en cuirasse" syringomyelic sensory alterations in cases of cervical spondylosis. Although the latter type of sensory change was exceptional, the former was seen not infrequently and usually consisted of areas of analgesia.

Quadrantic and hemicorporate patterns of sparing were seen in cases 1 and 3 respectively, and case 4 demonstrated relative sacral sparing of sensory deficit.

Sensory involvement-patterns not unlike a Brown-Séquard syndrome. Case 1 demonstrated this pattern reasonably well.

Presence of vague and indistinct borders to the sensory deficit. This phenomenon will not be considered unusual. It was particularly notable in case 2. In itself, it probably cannot be considered anything but a stage in the ascending or descending intensity of sensory alteration, which in turn depends upon the degree of compression and intrinsic sensory tract alteration.

Lack of confinement of upper limb involvement to familiar cervical dermatome distribution. Brain and associates[6] observed that when the upper extremities were involved, frequently only the hand and distal forearm showed the alteration. Spillane and Lloyd[7] noted the lack of confinement of sensory alteration to cervical root distribution and found the fingers rather evenly affected bilaterally. Unusual patterns were seen in our cases 1, 2, and 5.

Sensory alteration in dermatomes lying segmentally above the site of cord compression. In the only case in which this was noted (case 4) the surgeon found no release of free cerebrospinal fluid flow until the lamina of C3 was removed. The mechanism of cord distortion at a distance might be a factor in the production of sensory alteration cephalad to the compression. Such alterations above the level of compression are less readily understood than

those occurring at a distance below, a frequently occurring motor counterpart of the latter being the presence of interosseous muscle atrophy in association with mid- or upper cervical cord compression. Little has been noted concerning this phenomenon of alteration above the compression that we have been able to find. Spillane and Lloyd[7] studied one patient in whom the sensory alteration apparently extended up to C3. It must be admitted that multiple sites of cord compression other than those demonstrated by operation may account for certain of these unusual patterns.

Perversion of thermal or pain stimuli. We observed perversion of thermal stimuli in cases 3 and 5. It was particularly notable with respect to perception of cold which was more often interpreted as hot by the patient. Attention was called to this distortion or perceptional defect by Symonds and Meadows[4] in 1937.

The mechanisms whereby all these varied changes may come about are not fully understood. The cord may be distorted and stretched by the tumor mass and the suspending dentate ligaments. Such a mechanism was suggested by Abrahamson and Grossman[1] and later championed by Kahn[9] who demonstrated the rationale of releasing the dentate ligaments in the face of anterior cervical cord compression. The lines of stress within the cord might explain certain tract dysfunction, varying with the compromising force or its direction of application. The wide separation of certain tracts would explain some forms of sensory dissociation, and the existence of several pathways subserving the same sensibility would explain others. When sensations whose conducting tracts are believed to lie in juxtaposition (such as pain and temperature) are dissociated, then the concept of differential susceptibility to compression and anoxia may be introduced. In fact, such a concept may explain to better advantage phenomena elucidated by other mechanisms previously noted. Such a concept is not without physiologic support in the study of neural impulse conduction of peripheral nerves.[9] The dissociation of vibration sense and postural sense noted in syringomyelia has been used by Netsky[5] to support the concept that pallesthesia is conducted by way of the lateral columns of the cord. More evidence is required than mere perceptional dissociation to divorce vibratory sense conduction from its generally accepted posterior column location; we still closely associate pain and temperature sense conduction topographically, and yet these sensations may be distinctly dissociated clinically.

Compression of vascular structures of the cord may conceivably be responsible for certain of the bizarre patterns of sensation observed. Allen[8] observed that cord compression was often not great and that the selectivity of sensory involvement was explicable on a vascular rather than a compressional basis. Although this is an attractive thesis, it requires further morbid anatomic study.

We have tended to separate sharply the sensory alterations suggestive of extramedullary disease and intrinsic cord disease in this discussion. Yet, as Brain and associates[6] have clearly demonstrated in their six cases of postmortem study of cervical spondylosis, there are intrinsic cord changes in the direction of long tract degeneration and softening – truly an intramedullary sub-

stratum for the observed defects.

A second factor worthy of emphasis is that protrusions which are demonstrated surgically may appear as isolated lesions. However, multiple protrusions may exist, and while some of these may show up on myelographic study others may not. The combination of several defects affording pressure upon the cord at varying sites may explain certain of the sensory patterns which are less readily understood if due to a single lesion.

The point which we would like to emphasize is that few sensory patterns can be accepted as indicating the exact nature of the cervical cord disease. Too often the sensory picture misleads us regarding both the site of disease and its nature. If we will also realize that cervical spondylosis may masquerade as other forms of degenerative disease of the cervical spinal cord, we will push our investigations vigorously and salvage certain patients from prolonged disability, once the cervical locale of disease has been incriminated.

SUMMARY

A group of five clinical case studies of cervical spondylosis with central disk protrusion and cord compression has served as a basis for an analysis of clinical aspects. Emphasis has been placed upon the varied sensory alterations encountered in such midline protrusions in the absence of clear radicular signs. Well demonstrated are examples of sharp sensory dissociations, relative trunk or sacral sparing, Brown-Séquard type findings, indefinite sensory margins and alterations of sensation above the level of cord compression, perversion of thermal stimuli, and unusual cervical dermatome deficit. It is suggested that once the cervical area of the spinal cord is suspected as the site of disease, the sensory patterns must not be given too much emphasis in ascertaining the nature of the disease process. Too often the varied manifestations of cervical intervertebral disk protrusion are mistakenly accepted as due to irremediable disease. Complete investigation of the nature of the process by ancillary technics will aid in accurate diagnosis and rational therapy.

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Toward a Neurology of Behavior

Roland P. Mackay, M.D.

NEUROLOGY, which began as a medical discipline, has intellectual and philosophic goals far beyond the elucidation and treatment of disease. Besides its practical medical applications in which we, as physicians, have particular interest, neurology is also a pure science directed toward the satisfaction of human curiosity. As such, it is an effort to understand and describe the nervous system and its operations, not only in the minutiae of stimulation and response, but even in the broader field of the total adjustment of the organism to its internal and external circumstances. In these larger matters, the nervous system is the organ of behavior and, in a very real sense, the organ of mind, no matter what view one may take as to the nature of mind. Behavior, then, which is but the nervous system in action, offers the ultimate challenge to neurology, and neurology, when it accepts the challenge, becomes the boldest and most direct of man's answers to the ancient injunction, "Know thyself!" Let us consider for a short while where we now stand and how we may move toward a neurology of behavior.

Today our knowledge is already considerable. We understand that the nervous system takes stock of the environment and determines the organism's attitude and response. What is more wonderful, we know that in this process the traces of previous stock-takings exert controlling influence. We are familiar with some of the anatomic structures underlying this process – the afferent pathways, the thalamic and hypothalamic relays, the primary and secondary cortical sensory areas, the cerebellar and central nuclear masses which unravel the vast skein of incoming impulses and somehow re-knit them into appropriate patterns of outflow along efferent paths to fashion behavior.

Inevitably the cerebral cortex, as the most accessible portion of the central nervous system, received earliest attention from the days of Fritsch and Hitzig, Ferrier, and Hughlings Jackson, to the modern studies of Duser de Barenne and his followers with physiologic neuronography. The epic work of Penfield and Jasper on the surgical human patient added greatly to our knowledge and

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Presidential address read before the American Neurological Association, Atlantic City, June 14, 1954.

aided in the construction of a now familiar map of cortical functional centers. Eventually, however, refinements of the Horsley-Clarke stereotaxic instrument in the hands of many workers led to the study of deeper structures. Within the past 25 or more years we have become more acquainted with the nuclear centers around the third ventricle, and have learned something of the role of the "visceral brain," as MacLean[1] calls it, in serving as the central station to which the internal environment is reported and from which the infinitely delicate processes of homeostasis are controlled. We have learned a little also as to how external events as well are reported to the visceral brain and how complex hormonal and motor reactions are induced in the viscera, potentiating the extrinsic motor response and leading to an appropriate flow of subjectively experienced feeling and mood.

Many details of these reactions in the thalamic, hypothalamic, and other centers of the visceral brain have been worked out in one of the greatest of modern neurologic explorations by Ranson and his school, Bailey, Wheatley, Jasper, and Magoun and his collaborators, not to mention many others. For example, we know Magoun's ascending reticular activating system in the brainstem, which, receiving afferent stimuli, alerts the brain as a whole.[2] Lesions in this system in the hypothalamus, or its inhibition by a sleep center in the thalamus, permit sleep. Akinetic mutism, described by Cairns and others,[3] has been produced experimentally by Bailey and Davis[4] by placing lesions in the periaqueductal gray matter, possibly through destruction of a descending activating system. Anand and Brobeck[5] have found a feeding center in the lateral hypothalamic area, and a more medially placed abstinence or nonfeeding center. Other centers in the hypothalamic region control other visceral functions – the supraopticohypophyseal system controlling water metabolism through the neurohypophysis and its effects on reabsorption by the renal tubules; the predominantly cholinergic (parasympathetic) anterior portion of the hypothalamus, and the adrenergic (sympathetic) posterior portion which, when released from cortical controls, induces the familiar sham-rage; the interpeduncular nucleus, destruction of which was shown by Bailey and Davis to give the syndrome of obstinate progression;[6] and the hypothalamic controls over the thyrotropic, adrenocorticotropic, gonadotropic, and no doubt other tropic hormones of the adenohypophysis.

Despite these most impressive achievements, we are still far from a neurologic theory of behavior. The complexity of this brain, constituting an enormous city of cortical and subcortical centers, taxes the memory and imagination of even the most assiduous students. The concept of functions in centers has not been satisfying to all, and skeptics like Lashley have, in numerous contributions, cast doubt on the validity of many, especially in the cerebral cortex, in which topical ablations have demonstrated great capacity for substitutive function in whole or in part. Furthermore, experimental electrical stimulation, strychninization, and the surgical isolation of centers are unphysiologic in that they never occur in the normal animal. It is a legitimate technic to isolate and to stimulate artificially portions of the nervous system in order

to observe the unique function of each, but, aside from the artificiality of the process, such separate parts can scarcely function in isolation as they do in the intact animal. As pointed out by Walshe,[7] we learn by these methods only what we see happen under the conditions of the experiment and not what happens in normal circumstances.

What we need most of all is a method of studying the nervous system as a whole and in its several parts during normal behavior. The technic of recording potentials from the cortex during normal sensory stimulation or motor activity is an approach of this sort to the study of the intact animal. In particular, the simultaneous electrical recordings from numerous adjacent cortical points, as introduced by Lilly,[8] is a new and hopeful method by which shifting patterns of activity may be seen and recorded both in the resting and in the stimulated animal. But promising though these technics may be, they scarcely satisfy our great need for insight into the neurologic basis for behavior.

Attention must be directed, therefore, to the great body of knowledge available in the findings of classic psychology, which no unworthy allegiance to Descartian dualism should lead us to ignore. The clinical neurologist has long considered both the subjective experience and the objective behavior of his patients, greatly to his profit and understanding. With equal good fortune, we may fare as well. Let us consider, then, certain well known psychologic formulations and see, if possible, what they imply in a neurologic theory of behavior.

THE NEUROLOGY OF THE CONCEPT

In the first place, we shall have to explain in neurologic terms what in psychology is called the *concept* – the abstract summarization of the essential features of innumerable specific percepts. In a previous communication concerning memory, this matter was discussed in some detail.[9] For present purposes one may say that clusters of sensory items, often of diverse modalities but with a constancy despite variation in detail, are abstracted and somehow retained as generalizations in the nervous system. For example, out of the presentation of innumerable specific circles, one forms a generalization of the essence of them all – *circularity*. They may be presented visually, of all conceivable sizes, from the coccus under the microscope to the circumambient horizon; they may be viewed perpendicularly or obliquely; they may be seen in motion across the field of vision. They may be presented kinesthetically, as the center of the visual field traces their outlines through extraocular movements, or when worn as rings on the fingers, or palpated as circular disks, or traversed on foot as circular paths, or drawn with a compass on paper. Out of all these variant presentations comes the generalized abstraction, the concept, circularity, which at length may be extended to include a "circle" of friends, or circular reasoning, or the "vicious circle" of causality. Thus, the concept, circularity, is not visual or tactile or kinesthetic alone; it is compounded out of the topographic and temporal order in which the sensory items appear. For another example, out of innumerable presentations of specific

hats one forms a summarization or abstraction of hat. This concept includes many sensory modalities: visual, tactile, proprioceptive, even olfactory. But its essential feature is a spatial and temporal order in which the sensory items of any or all of the modalities impinge upon the sensorium.

The concept, then, a sensory generalization, is the template or standard or pattern by which new sensory presentations are judged as to whether they be circles, hats, or what not. Obviously, clusters of sensory items can become percepts only as they are generalized in concepts. Now it is evident that when a new hat or circle is presented, its concordance with the concept leads to its perception as hat or circle. This is the process of recognition – a process of the agreement of the unique spatial and temporal order of a newly presented cluster of sensory items with the generalized order of the concept. But psychologically recognition is a subjective experience, characterized, it would seem, by an affective *feeling* of familiarity, of *déjà vu*, if you please. In addition, the experience at this point includes the affective or emotional attitude to the object recognized – pleasure or displeasure, liking or dislike – followed by the appropriate extrinsic behavior.

It is at once apparent that the formation of concepts begins at birth, and that no subjective order can be discerned in experience unless and until concepts are formed. Concepts, again, are under constant revision and amendment, subdivision and reclassification, as experience broadens and wisdom grows. The formation and refinement of concepts is, thus, the essence of learning, without which no cogent or meaningful apprehension of the environment can exist. Psychologically, these are elementary truths, but they are heavy with significance.

What can we say about the neurology of the concept? It is immediately obvious that the concordance of a cluster of sensory stimuli with an established concept cannot depend upon the activity of anatomically specific sensory pathways. There can be no specific neurons for the perception of hats, for example, considering how many sizes, shapes, colors, and kinds there may be, how their images may fall on any parts of the retina, and how they may be presented and recognized by vision, touch, or proprioception. Concordance must depend, rather, on the topographic distribution (shape) and sequential order (scanning, palpation, and so on) of the stimuli, and their "fit" with the topographic and sequential qualities of the concept. *The concept, in its neurologic representation, in turn, cannot reside anywhere as such, but must consist of specific neuronal sensitivities to a spatiotemporal pattern of stimulation.*

The nature of the sensitivities can scarcely be guessed; they are established by the repeated reception of the patterned stimuli of experience and their explanation awaits further knowledge of the intimate function of neuronal networks. We have a hint, perhaps, in the enduring sensitivities of receptor end-organs to specific stimuli – for example, auditory pitch, thermal state, qualities of odor, wave-lengths of light, and so on. These latter sensitivities, however, besides being themselves very poorly understood, are built-in and permanent. By analogy, one may remember how a radio receiver accepts only waves of

a frequency to which it is tuned or set, and wonder then whether the sensitivity of neuronal networks underlying the concept is a matter of a capacity for resonance to stimuli arriving in a specific distribution and frequency. Thus, the difficulty may be met of explaining how a single network – visual, for example – may have thousands of patterned sensitivities for as many concepts, since the permutations and combinations of distribution and frequency are well nigh infinite among even a few hundred neurons. So may an unlimited number of melodies be played on a single piano keyboard, and a vast literature be written with 26 letters of the alphabet. Further, however, we need information on how neuronal nets acquire abstracted patterns of receptive sensitivity from repeated patterns of stimulation. This process of sensitization is the process of learning – of the formation of concepts. The retention of the patterns of sensitivity is memory. Their decay and loss is forgetting.

We need a new word for the specific sensitivity of a neuronal network for patterns of incoming sensory impulses – a neurologic term corresponding to the psychologic "concept." Since we are speaking of a pattern of receptive sensitivity, I suggest the term *esthesotype.**

Upon the concordance of the pattern of incoming stimuli and the esthesotype, subjective recognition occurs, a process accompanied by and, I believe, dependent upon an affective feeling of familiarity. This fact suggests that, upon concordance, the neuronal activity gains access to the affective centers in the diencephalon. There the process may be assumed to evoke also the autonomic response to the percept, with its emotional correlate, and so lead further to the extrinsic motor response as well. Throughout this whole complicated chain of reactions, it seems inescapable that the spatiotemporal pattern of stimulation is the key which unlocks one receptive door after another, on to the final act of the extrinsic response.

The problem of selective activation, though troublesome, illuminates this question of the neurology of the concept. For example, a young mother sleeps soundly through meaningless noises, but awakens with a start at the first cry of her baby. In this instance, incoming stimuli remain quite ineffective until one group "fits the pattern" of the concept–baby. Neurologically, in the sleeping mother, the ascending reticular activating system is inactive and only the concordance or "fit" of stimulus-pattern with the esthesotype for baby allows the auditory stimulus access to the activating system and to the hypothalamic autonomic structures. The spatiotemporal pattern of sensitivity has already been acquired by the mother's previous experience with babies and particularly with her baby, accompanied by the subjective emotional overtones. The esthesotype, baby, has, by this experience, been invested with importance – that is, the pathways to the autonomic centers are open to a set of stimuli in the concordant pattern. The key, if it fits, opens the lock. In common language, the mother has invested her baby's cry with importance and is alerted when it occurs. In psychologic terms, the stimulus conforms to the concept and af-

*From the Greek *aisthesis*, "sensory perception" and *typos*, "pattern."

fective recognition and emotional response follow. In neurologic terms, auditory afferent impulses have a spatiotemporal pattern which "fits" the pattern of receptive sensitivity – the esthesotype – to gain admission to the activating system and the hypothalamic autonomic centers and initiates the whole autonomic and motor response.

NEUROLOGY OF CHARACTER

In the second place, for the construction of a neurology of behavior we need a neurologic explanation for the character of the individual. There is a constancy in the behavior of every person, less notable in the young, more obvious in the mature. Upon observing the act of a friend, we say, "How like him to do that!" for the new act is in accord with his previous ways. In each of us a motor retentiveness preserves our original traits but leaves their amendment possible with changing experience. Ultimately, neurology must account for this remarkable retention and modification of patterns of response which underlie the constancy and growth of character.

The stability of motor behavior is best examined in its simplest form. For example, the inscribing of one's signature, so laboriously learned in childhood, represents a motor memory, based on a neurologic pattern to which I have applied the term *kinemnesis.*[9] Every signature of mine is recognizably the same, yet each is recognizably different in finer detail. It is evident, I think, that each inscription is but a specific expression of a motor pattern which is enduringly retained. Similarly, each time I ride a bicycle, throw a baseball, whistle a tune, I give specific, unique expression to a remembered motor pattern – a kinemnesis. This kinemnesis is thus the motor homologue of the sensory concept (or its underlying esthesotype) – a generalized abstraction of innumerable specific acts, just as the esthesotype is a generalized summary of innumerable patterned clusters of afferent stimuli. It is a spatial and rhythmical pattern, like a musical score, repeatedly expressible in single performances, no two of which are quite identical. At higher levels, kinemneses become most complex and constitute character traits. Each of us has his own pattern of response to aggression, to conciliation, to affection, to hate. Character then, is the aggregate of one's kinemneses.

Before we can have a neurology of behavior we must explain the mechanism of the kinemnesis. Like the concept, the kinemnesis cannot be recorded in anatomic, neuronal "grooves." This is obvious since no two acts are precisely alike, but each is a unique expression of the generalized pattern. One does not use the same effector units twice, to exactly the same degree, in exactly the same sequence in signing his name or in any other act. The kinemnesis must consist, on the contrary, of an ordered pattern of neuronal activity, each step of which leads to the next through selective sensitivity, but not through identical synaptic connections. It is obvious, further, that the kinemnesis in complex skills involves intricate chain reactions, and that these accom-

[9]From the Greek *kinesis,* "movement" and *mneme,* "memory."

plish a close control of the sequence by newly in-coming and correcting information – as, for example, during the fielding of a bounding grounder by a shortstop who corrects for each erratic movement of the ball and decides eventually whether to throw to first base or second in accord with the varying possibilities for a double play. To compare the performance of a beginner with that of a skilled player demonstrates conclusively that such kinemneses are acquired and retained as a result of experience.

No one can yet suggest a solution to the problem of the nature of the kinemnesis, how it is established through experience, and how it is retained and modified. But to understand the effector side of behavior in neurologic terms we must study not so much nuclear centers as patterns and sequences of motor discharge. We shall need to consider frequencies of neuronal activity, the possibilities of resonance, interference, damping, and summation. All this must somehow be done in the intact animal, subjected to physiologic stimuli. Above all, we need to know how experience modifies neuronal sensitivities (that is, how we acquire skill) and how these sensitivities (and skills) are retained, and how with disuse they may slowly decay. This vast field is "white unto the harvest" and awaits our investigative ingenuity and our most reflective analysis.

SUMMARY

In summary, if we can come to understand the neurology of the concept on the one hand, and of the character of the individual on the other, we shall have progressed far toward a neurology of behavior. Our discussion here suggests that, in both instances, we come down ultimately to the problem of interneuronal sensitivities. This resembles the old problem of the nature and specificity of the synapse, but now enlarged to reject the rigid "engram" or "groove" theory in favor of a broader, more flexible theory of patterns of receptivity and response in large neuronal networks. Thus, the concept is considered to depend upon a spatiotemporal pattern of selective receptivity or sensitivity of large populations of neurons toward the patterned inflow of impulses from all parts of the sensorium. When the pattern of impingement "fits" a pattern of receptivity the inflow secures access to, and activates, the diencephalon with the psychologic experience of familiarity and recognition, and the appropriate visceral (and emotional) response. The neuronal pattern of sensitivity I have called the *esthesotype*.

The diencephalic activation affords the dynamic for the extrinsic motor response, which again is achieved by effector motor units, stimulated in a spatiotemporal pattern of activity which I have called the *kinemnesis*. Tentatively, one must assume that the kinemnesis is a pattern of neuronal discharge, even as the concept (or its neurologic homologue, the esthesotype) is a pattern of neuronal receptivity, and that the kinemnesis is activated by the total sensory inflow in its perceptual pattern. Once activated, the network of effector neurons discharges in the spatiotemporal pattern of the evoked kinemnesis.

The most intriguing problem of all is to discover the mechanisms of patterns of sensitivity and response in neural networks, and specifically how the patterns are established, reinforced, and modified by the experiences and activities of life. Only a consideration of the nervous system as a whole can solve problems of this sort and lead toward a neurology of behavior.

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But in this disease there is one circumstance which demands particular attention; the long period to which it may be extended. One of its peculiar symptoms, Scelotyrbe festinans, may not occur until the disease has existed ten or twelve years, or more; hence, when looking for the period, within which our hopes of remedial aid is to be limited, we may, guided by the slow progress of the malady, extend it to a great length, when compared with that within which we should be obliged to confine ourselves in most other diseases.

James Parkinson in *An Essay on the Shaking Palsy*, published in 1817.

Significance of Negative Neurosurgical Diagnostic Studies

F. A. Martin, M.D., J. E. Webster, M.D. and E. S. Gurdjian, M.D.

IN ORDER TO DETERMINE the accuracy of neurosurgical diagnostic procedures, 200 verified intracranial mass lesions were reviewed.[3] These procedures include pneumoencephalography, ventriculography, and angiography; 236 studies, of which 42 were normal (18 per cent), were performed on these two hundred patients. Thirteen of 82 pneumoencephalograms, five of 96 ventriculograms, and 24 of 58 angiograms were reported negative.

It was possible in all cases to determine the site of the lesion during life. The manner in which the diagnosis was established was evaluated. It was found that patients could be placed in three groups. From each of these groups, five representative cases were chosen for presentation.

Group 1 consists of those patients who had negative pneumoencephalograms and/or angiograms and who were diagnosed on the basis of clinical studies or survey roentgen examinations.

Group 2 consists of patients with negative angiograms, who were then studied by means of pneumograms which were diagnostic.

Group 3 consists of those patients who were studied by several methods, all of which were negative early in the course of the disease but were positive upon restudy at a later time using the same methods.

GROUP 1

Case 1.—A 38 year old woman was admitted on January 11, 1948 with a complaint of a mass in the left frontoparietal area. Examination at that time revealed a 6 cm. mass in that area, and routine roentgenograms showed an erosion of the left frontal and parietal bones extending downward toward the base. Electroencephalography revealed a focal abnormality in the left frontoparietal area. Pneumoencephalography was negative. A large globular outer convexity meningioma was removed (figure 1).

Case 2.—A 66 year old man was admitted on July 31, 1951 with a chief complaint of right-sided convulsions. Examination revealed a right Babinski reflex and a partial aphasia. The routine roentgenograms showed a questionable shift of the pineal gland to the right side. There was a left frontotemporal electroencephalographic focus. A left percutaneous

This work aided by the Kresge Fund.
From the University Neurosurgical Service, Grace Hospital, Detroit, Michigan.
Read at the seventy-eighth annual meeting of the American Neurological Association, Atlantic City, June, 1953.

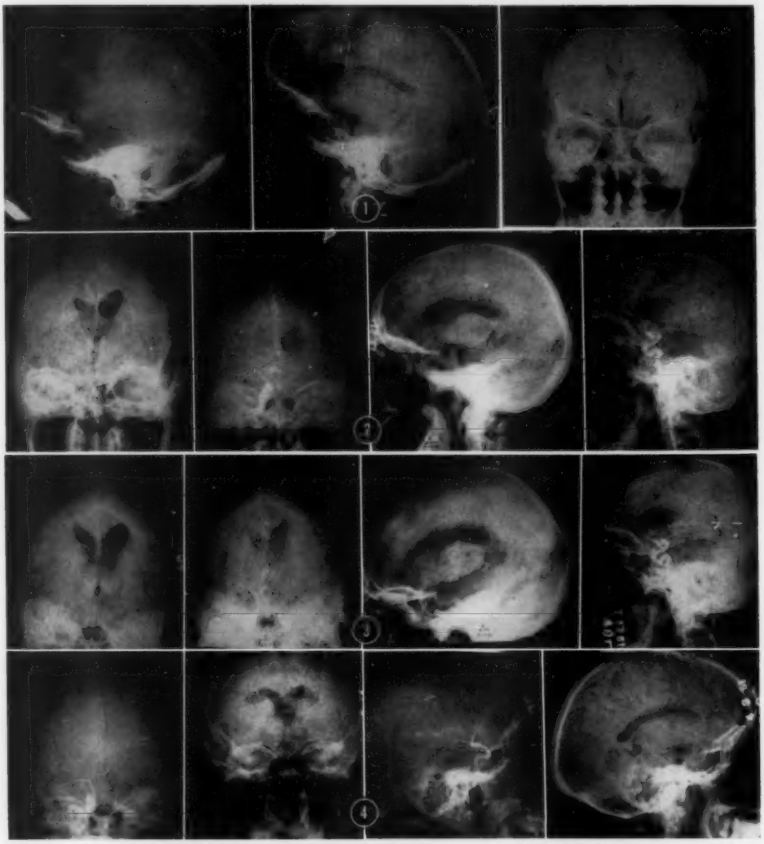


FIG. 1. Case 1—group 1. The upper left lateral roentgenogram of the skull shows hyperostosing and cystic changes of the frontal bone on the left side. The air studies shown are entirely negative and did not reveal the presence of a globular meningioma of the left frontal region.

FIG. 2. Case 4—group 1. This patient had jacksonian seizures of the left half of the body and the air studies above suggest a possible mass in the parietal area on the right side. The angiograms were considered to be essentially negative.

FIG. 3. Case 4—group 1. Admitted about six months later showing more clearly that there was a mass in the right parietal area with negative angiograms. This patient had a large astrocytoma of the Sylvian area on the right side.

FIG. 4. Case 5—group 1. This patient with right optic atrophy had negative air studies and angiograms with satisfactory filling of the basal cisterns in the lateral view. A pituitary adenoma was found at operation.

angiogram and a pneumoencephalogram were not diagnostic. The patient refused exploratory surgery and was discharged. He was readmitted on October 1, 1951 with a right hemiplegia, confusion, aphasia, and increased frequency of seizures. The electroencephalogram revealed an abnormality now spread over the entire left hemisphere. The patient's

condition was considered critical and surgery was carried out. A large left temporoparietal glioma of unclassified type was found.

Case 3.—A 47 year old woman was admitted August 20, 1952 with a chief complaint of pain in the suboccipital region and high cervical region of four years' duration, which had become more intense in the past several months. She gave a history also of ataxia when she looked upward and she staggered to the right on some occasions. Examination revealed only a slight weakness of the left arm and left leg. Myelography, pneumoencephalography, and ventriculography were all negative. There was a bilaterally symmetrical grade 2 dysrhythmia in the electroencephalogram. A suboccipital craniectomy was suggested, but the patient declined surgery. The patient was readmitted on October 6, 1952 with an accentuation in the suboccipital pain and increased ataxia now associated with vertigo, confusion, diplopia, and dysphagia. Examination at this time revealed a confused patient with left hemiparesis and a Babinski reflex on that side. There was astereognosis of the left upper extremity. The patient fell to the right side on the Romberg test. Ventriculography was repeated and again was found to be negative. An exploratory suboccipital craniectomy was now permitted and was performed on October 14, 1952. This revealed a meningioma at the base beneath the medulla which extended from the craniocervical junction superiorly as far as the incisura.

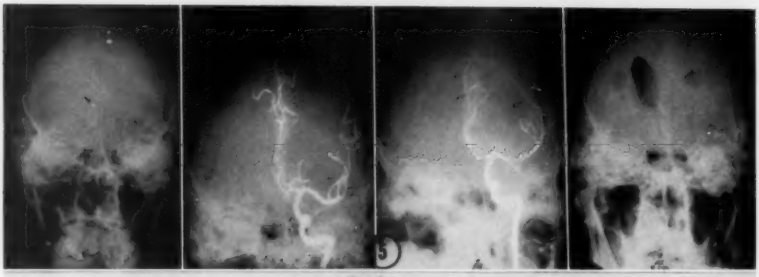
Case 4.—A 51 year old man was admitted in January 1951 with a complaint of convulsions involving the left side of the body and occasionally limited to swallowing movements. Other than a minimal left seventh nerve palsy, examination was negative. Studies by electroencephalography and right percutaneous angiography were negative. Pneumoencephalography was suggestive of a mass in the right parietal area. The patient refused surgery at this admission. His complaints became worse and he was readmitted in July 1951. Again angiography and electroencephalography were negative. However, the pneumoencephalogram revealed slight progression in the distortion of the ventricular system by a mass. Surgery revealed an astrocytoma of the right Sylvian area (figures 2 and 3).

Case 5.—A 26 year old woman was admitted March 19, 1951 complaining of progressive loss of vision of the right eye. Examination revealed a right primary optic atrophy. Routine roentgenograms showed an erosion of the sella turcica and of the posterior clinoid processes. Studies by right percutaneous angiography and pneumoencephalography were negative. A subtotal excision of a pituitary adenoma was performed (figure 4).

GROUP 2

Case 1.—A 46 year old man was admitted on January 6, 1951 with complaints of formed flashes of light of three months' duration. Examination revealed a right homonomous hemianopsia and a right central seventh nerve palsy. Electroencephalography showed a focus in the left occiput. A left percutaneous angiogram was negative, as was the pneumoencephalogram. The patient declined surgery and was discharged. He was readmitted on April 21, 1951 with added complaints of confusion as well as continuation of his previous symptoms. The entire left hemisphere now produced abnormal electroencephalographic patterns. Ventriculography revealed a left occipital mass which at operation proved to be a glioblastoma.

Case 2.—A 52 year old man was admitted April 24, 1952 because of headache and vertigo of sudden onset and a short period of weakness of the right side of the body. The cerebrospinal fluid was bloody. The examination revealed loss of vibratory sense over the right side of the body. Routine roentgenograms revealed a shift of the pineal gland to the right side. A left temporoparietal focus was obtained in the electroencephalogram. A left percutaneous angiogram was negative. The patient declined further studies. His symptoms continued and he developed a right hemiplegia. On readmission May 2, 1952, the electroencephalogram had not changed and again angiographic studies were normal. Ventriculograms performed at this time, however, revealed a left temporoparietal mass which proved to be a glioblastoma (figures 5 and 6).



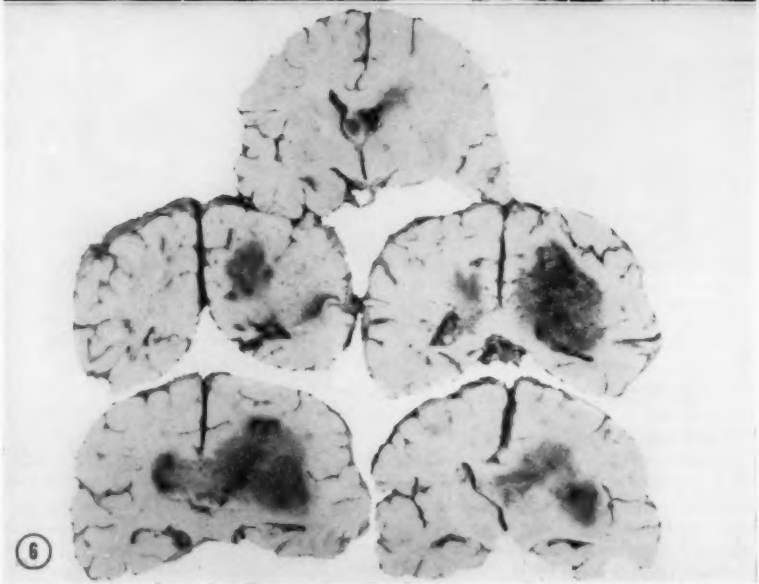


FIG. 5. Case 2—group 2. The left roentgenogram is suggestive of a pineal shift to the right. The angiogram was found to be essentially negative. The angiogram to the right is still negative on a subsequent admission about a month later. The ventriculogram on the right shows a large parietotemporal mass lesion, three months later.

FIG. 6. Case 2—group 2. Sections of the brain reveal a large glioblastoma which involved midline structures.

Case 3.—A 49 year old man was admitted with generalized seizures of recent origin. There was no physical evidence of neurologic disease. The routine skull roentgenograms revealed radiopaque deposits in the right middle fossa. Right percutaneous angiography was negative. There was a suggestion of obliteration of the right temporal horn on pneumoencephalography. Surgical exploration revealed an astrocytoma in the right temporal lobe.

Case 4.—A 22 year old woman was admitted in November 1951 with a history of headache, nausea, and vomiting of two months' duration. Examination revealed a right seventh nerve weakness and hemihypalgesia. A left parieto-occipital delta focus was found

FIG. 7. Case 5—group 2. The angiograms are essentially negative. The ventriculogram shows a huge mass in the right parieto-occipital area.

FIG. 8. Case 5—group 2. The posterior placed glioblastoma seen here is the portion remaining after wide surgical excision.

in the electroencephalogram. A left-sided angiogram was normal. The ventriculogram, however, was diagnostic of a space-occupying mass in the parietal lobe. This was a verified glioblastoma.

Case 5.—A 36 year old woman was admitted February 14, 1953 with complaints of left hemiplegia of sudden onset. The cerebrospinal fluid was normal. The electroencephalogram revealed a right parietotemporal focus. A right percutaneous angiogram was negative. A pneumoencephalogram was a technical failure due to insufficient filling of the ventricles. A ventriculogram localized a right deep parietal mass which on biopsy was a glioblastoma (figures 7 and 8).

GROUP 3

Case 1.—A 60 year old woman was admitted May 22, 1950 with a chief complaint of left frontal headache. Examination revealed a partial, sensory type aphasia. Both the headache and the aphasia were sudden in onset. An electroencephalogram showed a left temporal focus which was confined entirely to this area. A left angiogram appeared normal. The patient was readmitted June 30, 1950 in the same state and with the same complaints. At this time pneumoencephalography was performed and found to be normal. The patient was discharged and later readmitted on September 18, 1950 with right hemiparesis and a more complete aphasia. The electroencephalographic focus had persisted in the left temporal area. Pneumoencephalogram at this time revealed a mass in the left temporal area which proved to be a glioblastoma. Seventeen weeks had passed since the initial study was performed.

Case 2.—A 48 year old woman was admitted to another hospital in December 1945 with a complaint of unilateral seizures. Routine roentgenograms showed a few small,

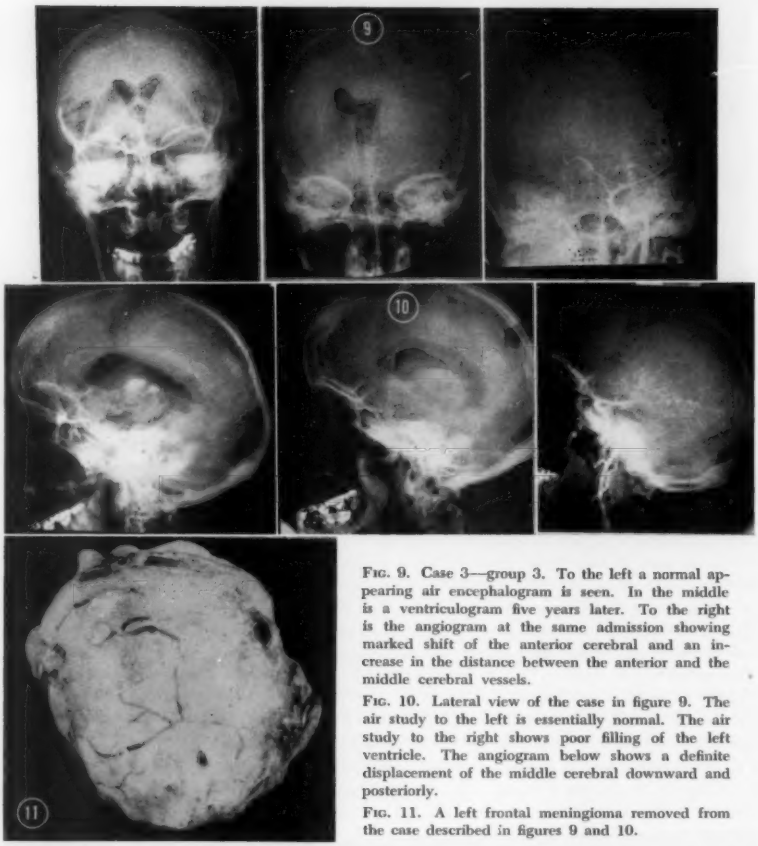


FIG. 9. Case 3—group 3. To the left a normal appearing air encephalogram is seen. In the middle is a ventriculogram five years later. To the right is the angiogram at the same admission showing marked shift of the anterior cerebral and an increase in the distance between the anterior and the middle cerebral vessels.

FIG. 10. Lateral view of the case in figure 9. The air study to the left is essentially normal. The air study to the right shows poor filling of the left ventricle. The angiogram below shows a definite displacement of the middle cerebral downward and posteriorly.

FIG. 11. A left frontal meningioma removed from the case described in figures 9 and 10.

barely discernible calcifications in the right parietal area. A pneumoencephalogram, however, appeared normal. The patient was readmitted on May 23, 1948 because of increased frequency of seizures. Again a pneumoencephalogram was considered normal. The patient was discharged and readmitted on July 14, 1948 with seizures and confusion. A right temporal parietal focus was noted on the electroencephalogram. At this time a pneumoencephalogram was diagnostic, revealing a mass in the right parietal lobe which proved to be an astrocytoma. Three and one-half years had elapsed between the initial study and the final diagnostic study.

Case 3.—A 54 year old woman was admitted on August 19, 1946 in status epilepticus. A left central delta focus was noted on the electroencephalogram. A pneumoencephalogram was normal. The patient was discharged and readmitted on December 9, 1952, again in status epilepticus, with an aphasia and confusion. A left temporal focus was noted in the electroencephalogram appearing more superficial in its origin. A left angiogram suggested a frontal mass. The ventriculograms were diagnostic and craniotomy revealed a meningioma of the midline frontal area on the left side. Five years and three months had passed

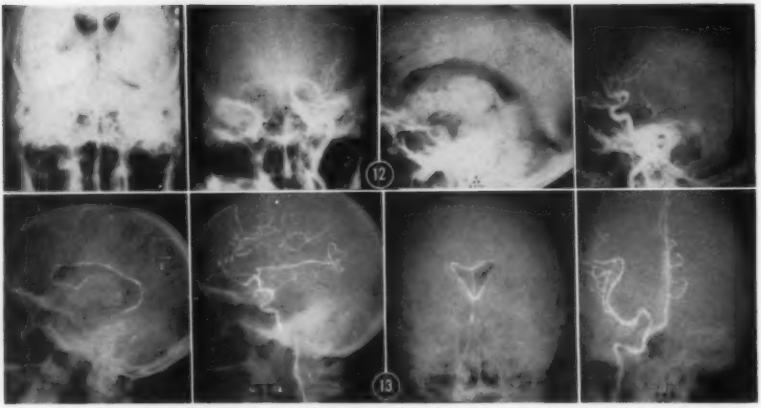


FIG. 12. Case 4—group 3. The anteroposterior and lateral views of the air encephalogram are essentially negative. The angiograms six months later show a mass in the temporal region on the left side.

FIG. 13. Case 5—group 3. In June 1952 the air studies and angiograms were thought to be negative. There is a slight inbending of the body of the ventricle and some compression of the pericollosal vessel in the lateral view. Compare these figures with figures 14 and 15.

from the time of the initial study to the conclusive diagnostic studies (figures 9, 10, and 11).

Case 4.—A 52 year old man was admitted February 28, 1952 with the complaint of five attacks of generalized seizures during a 14 month period. A left temporal delta focus was noted in the electroencephalogram. A pneumoencephalogram was within normal limits. The patient was discharged, to be readmitted on October 2, 1952 with increased frequency of seizures, confusion, and aphasia. A spread of the focus over the entire left hemisphere was noted in the electroencephalogram. A left angiogram revealed a mass lesion in the left temporal lobe which proved to be a glioblastoma. Eight months had passed from the initial study to the diagnostic study (figure 12).

Case 5.—A 49 year old man was admitted to another hospital in June 1952 because of sensory seizures occurring in the left leg. The electroencephalogram, angiograms, and pneumoencephalogram were reported negative. Reviewed in retrospect, the films from this hospital perhaps were not within normal limits, but they could not be considered diagnostic. The patient was admitted to this neurosurgical service in December 1952 with a left hemiparesis, occasional generalized seizures, and paraesthesias of the left leg. The patient also experienced chest pain following an accident which caused a fracture of right wrist as well as contusions to the chest. A generalized gross dysrhythmia was noted in the electroencephalogram. A right-sided angiogram and a pneumoencephalogram suggested a mass lesion. Exploratory surgery was planned but the patient's chest and cardiac symptoms resulted in postponement of surgical treatment. He was readmitted on January 21, 1952 with a progression of the neurologic symptoms, but with apparent improvement in cardiac status. Examination at the time of admission revealed left hemiplegia, aphasia, and confusion. A grand mal seizure occurred in the hospital. A right-sided angiogram and a ventriculogram revealed a right parasagittal parietal mass. While awaiting surgery, the patient expired from a coronary occlusion. The autopsy revealed a right parasagittal parietal glioblastoma and a cerebral infarct. At least seven months had passed from the time of onset of his disease until diagnostic angiogram and air studies were obtained (figures 13, 14, 15, 16, and 17).

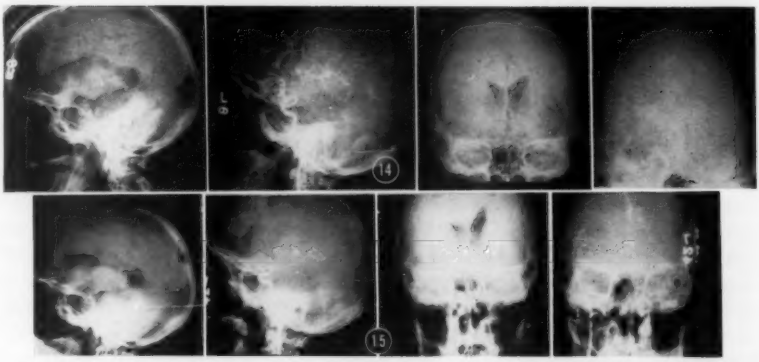


FIG. 14. Case 5—group 3. Air studies and angiograms six months later showing a more definite deformation of the body of the ventricle in the lateral view and a bending of the pericollosal vessel in its course more posteriorly, seen in the lateral angiogram. Compare this figure with figures 13 and 15.

FIG. 15. Case 5—group 3. Note the marked deformation of the right lateral ventricle, the shift of the ventricular system to the left in the ventriculogram. The angiograms show some downward deformation of the middle cerebral in the lateral view. The anterior cerebral could not be visualized in this view. In the anteroposterior view the angiogram does not look convincingly abnormal.

DISCUSSION

Alterations in the ventricles, the subarachnoid spaces, and the vessels brought about by the presence of a space-occupying mass are produced by one or both of two mechanisms. These are: 1) application of direct pressure against the vessels or the cavity, and 2) filling of abnormal channels.

Direct pressure against a vessel or cavity produces one or several of the following results: 1) displacement, 2) deformation, 3) obliteration, or 4) dilatation. Thus, a temporal lobe glioma may displace the middle cerebral artery upward or shift the ventricular system toward the opposite side. An olfactory groove meningioma may obliterate the anterior cerebral artery and

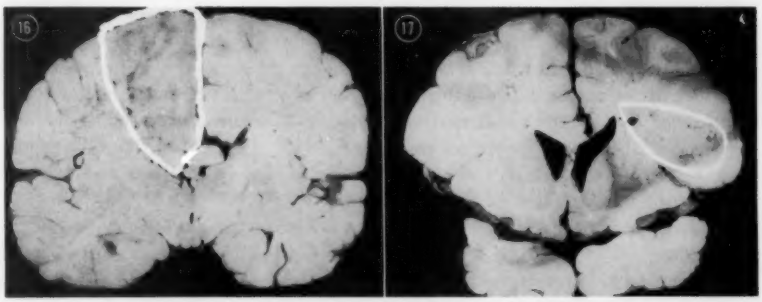


FIG. 16. Case 5—group 3. A glioblastoma was found in the right hemisphere.

FIG. 17. Case 5—group 3. This picture reveals an infarct of the left hemisphere of the same brain pictured in figure 16. This pathology was not detected by diagnostic studies.

deform the anterior horn of the lateral ventricle. Commonly seen in the hemispheric lesions is the dilation of the contralateral ventricle due to obstruction of the foramen of Monro.

Occasionally a cystic tumor which communicates with the ventricles may fill with air. Since the widespread use of serial angiography, filling of the intrinsic vessels of a tumor is now more commonly observed.

The question arises as to the size a tumor must attain before these mechanisms alter relationships in the roentgenograms. The volume of the mass apparently is not the crucial factor. More important is the site at which the mass occurs and the response of the normal tissue to its presence. A small mass adjacent to ventricles or vessels will probably alter them early in its growth. Common examples are those tumors which occur in close proximity to the aqueduct of Sylvius or the circle of Willis. When a tumor causes swelling of the cerebral tissue, structures remote from the actual mass itself may become altered. It is for this reason that diagnostic studies may be unreliable in determining the size of the lesion.

When a mass arises at a distance from the ventricles and larger vessels and produces minimal tissue reaction, it may attain a larger size before becoming roentgenographically detectable even though the patient may present severe disability. Two of our cases, an early glioma of the paracentral gyrus and a parasagittal meningioma, caused only minimal deformation of the posterior superior aspects of the homolateral ventricle. Such a minimal defect may be mistaken for the normal irregularity of the ventricle caused by the cingulate and paracentral gyri.

In the growth cycle of a tumor the time at which the surgeon will be allowed to perform a diagnostic procedure, the site at which a tumor may occur, and the response of the surrounding tissues to that tumor, all may influence the diagnostic evaluation of a given patient. Other factors which contribute to the occurrence of erroneous diagnoses are: 1) insufficient filling of the structures with media, 2) malpositioning of the patient during roentgenography, and 3) limited experience of the observer.

Insufficient filling of structures may be corrected by repetition of the study. A common source of error is poor filling of the basal cisterns in a pneumoencephalogram and the peripheral branches of the middle cerebral complex in an angiogram. Failures may occur in the pneumoencephalogram because of the use of small quantities of air. Failures in angiography may occur because of poor coordination between the operator and the technician resulting in premature or delayed exposure of the film. Thus the intrinsic vasculature of a tumor may not be recorded.

It is important to obtain an accurate anteroposterior or posterioanterior roentgenogram at all times, if slight shifts of the ventricles or anterior cerebral vessels are to be appreciated. Filling of the fourth ventricle may sometimes be obtained by positioning the patient so that the air may enter this area.

Of all factors the most difficult to control is the human element. There is a tendency to interpret minimal defects as normal variations. A difference

in the size of the lateral ventricles, slight invagination of the ventricles, and minimal shifts of the vessels may be difficult to appreciate.

It is recognized that certain mass lesions in the cranial cavity produce such characteristic clinical syndromes that the diagnosis is clear and operative diagnostic procedures are not necessary. Cerebellopontine angle tumors, pituitary adenomas, patients with Jacksonian seizures, homonomous field defects, certain patients with brain stem involvement, and cases with osteolytic and hyperostosing bone lesions, pressure erosions, and abnormal calcifications are examples. Undoubtedly, in many such instances, operative intervention may be decided upon without further evaluation by diagnostic technics.

When diagnostic neurosurgical procedures are negative in an acutely ill patient in whom clinical localization is indefinite, further immediate evaluation by another method appears indicated. Tumors of the middle or posterior third of the hemispheres not detected by carotid angiograms become apparent on pneumoencephalograms and ventriculograms. Because the basal cisterns are not filled when air is introduced directly into the ventricles, a small neoplasm in this region may be undetected unless pneumoencephalography is used. Tne use of angiography may reveal an angioma not sufficiently large to be appreciated in a pneumoencephalogram.

When negative studies are obtained in the brain tumor suspect with minimal neurologic disability, he may be observed for varying periods of time and restudied. The frequency of observation and interval of time necessary must be determined on a clinical basis. The growth rate of the tumor appears to be the most important single factor which alters this time element.

SUMMARY

From a group of 200 patients with verified mass intracranial lesions, those with negative angiograms, pneumoencephalograms, and ventriculograms were selected and studied. They could be classified into three groups. Group 1 consisted of patients who had negative studies but who were operated upon the basis of clinical survey evidence. Group 2 consisted of patients who had negative studies of one type but who were restudied by other methods which proved to be diagnostic. Group 3 consisted of cases who had negative studies several times early in the course of their disease, which became positive after an interval of time had elapsed.

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Postconcussion Syndrome in Compensation and Litigation

Analysis of 95 Cases with Electroencephalographic Correlations

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THOUGH the clinical entity of the postconcussion syndrome is well known to all neurologists, there still occurs considerable difference of opinion by qualified experts when testifying in court as to degree of disability in these cases. It would seem that the usual triad of symptoms, headaches, dizzy spells, and emotional instability, is variously interpreted as either consequent to organic brain changes produced by the injury, or as an emotional reaction to the injury, the latter opinion being more often expressed when litigation or compensation benefits are at issue.

Evaluation of this problem is all the more difficult since objective neurologic findings in these cases are usually minimal or absent. The subjective complaints of the patient often seem exaggerated, are belittled by examiners and attorneys in an attempt to minimize the severity of the injury, and the patient is frequently looked upon as a neurotic or malingerer. The absence of prolonged unconsciousness following the head injury seems to carry great weight in such an opinion, and too often electroencephalographic recordings have not been performed. Cardiologists agree that one may have a significant cardiac lesion which can be recognized only by the electrocardiogram when physical examination of the heart is otherwise normal, and it is also well recognized that roentgen examination may detect lung disease despite the fact that routine examination is unrevealing. Among the 95 cases reviewed in this study, only the rare exception had an electroencephalogram previous to our examination. However, this did not deter qualified experts from expressing their opinion on the witness stand as to the presence or absence of brain damage.

It would seem that absence or minimal duration of unconsciousness, normality of the neurologic examination, and pending litigation or compensation benefits were the condemning trinity of factors in such an opinion. Is this

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Read by title at the sixth annual meeting of the American Academy of Neurology, Washington, D. C., April 29–May 1, 1954.

correct, and do the facts known about such cases support this view? Are we placing too much stress on certain criteria and too little on others? Can any other procedures help us in a correct interpretation in the individual case, and if so, are there limitations to the usefulness of such data?

In 1943, because of the need for control studies in cases of postconcussion syndrome, 100 cases of this clinical entity were reviewed, in which no compensation or litigation factors were present.[1] It was found that approximately 30 per cent of patients, despite apparently minimal head injury, had practically identical symptoms of headaches, dizzy spells, and personality changes for one year or longer following such injury; from 15 to 20 per cent still complained of these symptoms as late as three years after the accident. Motivation for financial gain was completely absent in these cases, which distinguished this group from those reported by other observers. Glaser and Shafer[2] found 31 per cent of 255 cases still suffering from these symptoms after five years, and Wechsler[3] was convinced that the persistent subjective complaints were due to a traumatic encephalopathy in 28 per cent of his series of 100 cases. Likewise Russell,[4] following up his series of 141 cases, found that 86, or 60 per cent, had persistent symptoms after six months, though only 14 of these cases were involved in pending litigation or compensation claims.

It would seem, therefore, that whether or not motivation for financial gain is present, postconcussion symptoms can certainly persist in a substantial percentage of cases (averaging 15 to 30 per cent) for three years or longer. It would seem more reasonable to look upon associated litigation or compensation as a possible aggravating factor, but not as a criterion of major significance in assessing the genuineness or degree of a patient's disability. It is not the prerogative of the expert medical witness to encompass the functions of judge and jury in addition to his own. Because a patient may have been emotionally unstable in the past, there is likewise no reason to attribute his persistent symptoms after an episode of cerebral concussion to a neurotic personality.

It was noted in the above mentioned study[1] that there had been no initial loss of consciousness or only momentary stunning in 20 per cent of these cases. Yet subjective symptoms of long duration persisted in these cases as frequently as in those where unconsciousness had occurred, regardless of duration. Other authors have confirmed these findings, where unquestioned severe brain damage has occurred without any loss of consciousness.[2–6] As is the case with a positive Wassermann reaction, a history of prolonged unconsciousness following head trauma is significant in evaluating residual brain damage, but the converse is not necessarily true.

PRESENT STUDY

Ninety-five consecutive cases of postconcussion syndrome were analyzed. In all these cases pending litigation or compensation factors were present, most of them having been referred to one of the authors in his role as an impartial specialist to the Workmen's Compensation Board, the Supreme Court

of New York, or various other legal agencies. Almost all showed normal neurologic findings, or at most, minor abnormalities of disputable significance. Electroencephalograms were performed in all cases, since this procedure had not previously been done in most cases. An attempt was made to diagnose each case clinically before the electroencephalogram and again after the procedure was completed, in the hope of determining criteria of correlation. The presence or absence of unconsciousness following injury, presence of hysterical symptoms, duration of symptoms since the accident were also studied and correlated with the electroencephalogram. Lastly, an attempt was made to determine whether any significant differences were present in these cases, as compared to the group in the previous study where litigation or compensation factors were absent.

ELECTROENCEPHALOGRAPHIC DATA

All recordings were made on an eight channel Medcraft electroencephalograph under standard procedure. To avoid possible differences in interpretation of borderline cases, only those records were considered abnormal which showed frequencies of less than seven cycles or more than 13 cycles per second. The latter frequencies, in addition, have an amplitude of more than 30 microvolts. Spike and sharp wave forms are found among the abnormal patterns. Burst activity describes sudden brief discharges of abnormal frequencies of higher voltage than the background activity. Amplitude asymmetry was so diagnosed when the voltage difference between two homologous areas was marked, the frequencies being within normal limits. Diffuse asymmetrical abnormal records were those in which the abnormal patterns were present over most areas bilaterally, but in which one side or one large area showed a greater degree of abnormal wave forms. Focal abnormalities were so interpreted when the abnormal activity was restricted to one or more adjacent electrodes, or, where the abnormality was pronounced in a single area, easily seen by inspection, although present to a lesser extent in adjacent areas or reflected in the opposite corresponding area.

For purposes of classifying the abnormal frequencies, four categories are listed : very slow (less than 4 cycles per second); moderate slow (4 to 7 cycles per second); moderate fast (13 to 22 cycles per second); and very fast (over 22 cycles per second). Table 1 summarizes the findings.

From this it is seen that definite abnormalities were found in about 55 per cent and borderline readings in 3 per cent of our series, figures approximately identical with those of other studies in cases of head injury with proved cerebral damage. Clarke and Harper[7] found abnormal records in 58 per cent of 186 soldiers with closed head injuries, and Weil[8] reported 53 per cent of abnormalities in posttraumatic brain injury with normal neurologic findings. Williams[9] studied 600 service personnel with similar chronic posttraumatic states and found that 50 per cent of them had abnormal records. Strauss, Ostow, and Greenstein[10] reported an incidence of 48 per cent of abnormal brain wave findings in their cases of proved cerebral damage. That this high

TABLE 1
SUMMARY OF ELECTROENCEPHALOGRAPHIC FINDINGS IN 95 CASES OF POSTCONCUSSION SYNDROME

	No. of Cases	*Per Cent*	*Moderate Slow*	*Very Slow*	*Moderate Fast*	*Very Fast*	*Bursts*	*Spikes*
Normal	40	42						
Borderline	3	3						
Abnormal	52	55						
a) amplitude asymmetry	3	3						
b) focal	32	33	28	4	2	1	10	13
c) diffuse								
1) symmetrical	11	12	9	1	1	0	4	2
2) asymmetrical	6	7	5	1	0	0	1	2

percentage of abnormality is the result of trauma is supported by the fact that focal changes were seen in 33 per cent of the total examined, and in 61 per cent of those with other abnormal findings. Focal abnormalities indicate structural cerebral damage, and have been shown to correspond with neurologic and roentgenographic evidence of such focal brain damage. Amplitude asymmetries are of equal significance, low voltage or suppressed activity having been found frequently in experimental and clinical studies of head injury.[11–13] Three of our cases showed such an abnormality.

The remaining 17 cases (19 per cent of the total, 33 per cent of the abnormal) showed diffuse changes, but in six of these asymmetries were also present. Furthermore, definite correlation with the site of injury was possible in half of the 41 cases showing focal or asymmetric changes. In the remainder it was not possible to obtain information as to the exact site of the injury and no attempt was made to correlate findings with injuries to the vertex or midline.

The types of records found are listed in table 1. About 80 per cent of the abnormal records showed moderate slow activity and 11 per cent very slow activity. Thus, slow activity is the most common pathologic finding; this has been found to be so in other studies of definite cerebral damage. Spike activity is found mainly in records showing focal abnormalities, being present in a little less than half of such cases. Fast activity is rarely seen.

Recent head injuries of less than three months' duration comprised a little less than a third of the total number of cases, and of these 50 per cent showed abnormal records, with focal findings in 35 per cent and diffuse asymmetrical changes in 15 per cent. Over two thirds of all cases, however, had injuries more than three months previously, and of this group about 58 per cent showed abnormal records, with focal changes in about 35 per cent, diffuse symmetrical in 17 per cent, diffuse asymmetrical in 3 per cent, and amplitude asymmetries in 3 per cent. Thus, in this series similar findings were present whether the head injury was recent or late, though individual variations may be found. This is in contrast to the findings in studies of severe head trauma, where electroencephalographic changes in more recent injuries were more pronounced because of the amount of cortical damage present, with later recovery or de-

struction of cerebral tissue causing improvement and return to normal.

Diffuse symmetric abnormalities in the later group, persisting from three months to four or five years after the injury, deserve special mention, because of the impression of some writers that such abnormalities are not due to the brain injury but to pre-existing abnormalities. In the later group 17 per cent of the abnormalities showed such findings. We are wholly in accord with Strauss, Ostow, and Greenstein[10] in their opinion that "such records indicate organic cerebral dysfunction" and are consistent with the brain injury sustained. Most of these cases show moderate slow activity. Williams[9] and many others have confirmed this opinion.

DISCUSSION

Though it is of clinical importance to know that 55 to 58 per cent of cases of postconcussion syndrome will show abnormal electroencephalographic records, the question arises whether one can predict from the history or the examination which patient will show such confirmatory evidence. In other words, how reliable is the clinical diagnosis before an electroencephalogram is made in determining whether the patient's subjective symptoms are due to organic brain changes or posttraumatic neurosis?

To help define our percentage of possible error in this regard, we attempted to predict, from our clinical impression of the case alone, whether the electroencephalogram would be normal or not. We found that such correlation was present in approximately 80 per cent of the cases. These 19 cases, which we might have interpreted incorrectly, merit further discussion. Definitely abnormal electroencephalographic findings were present in seven, whereas the clinical impression had been one of a functional state. In the remaining 12, the reverse was true since the electroencephalogram was normal, whereas clinically a true postconcussion state had been suspected. Some of these unexpected findings may be explained by the fact that in two cases more than one head injury had occurred in the past, and in one case a questionable history of old seizure disorder was obtained which might have been responsible for the abnormal records. Similarly, in the 12 cases with normal records where abnormal findings had been anticipated, four were associated with presumptive basilar skull fractures. In these cases the brain injury may have been a deep seated one where the electroencephalogram may not accurately reveal the lesion. Lastly, it must be recalled that many of these records were made two, three, and even four years after the head injury had occurred, and a certain amount of permanent brain cell destruction may have resulted in the interim. In such cases, the record would be unrevealing, since only functioning brain cells can yield such electrical activity.

The fact we wish to stress, however, is that one may be in error about 20 per cent of the time, if one attempts to assess these cases on the basis of history and examination alone, without the aid of the electroencephalogram. This fact alone should temper the testimony of the expert in head injury cases unless electroencephalographic records are available for the case.

As stated previously, the absence of unconsciousness following a blow to the head is often looked upon as evidence that the brain has not been injured in such trauma. In this series, 69 patients either experienced no loss of consciousness or were dazed for a few minutes following the head injury. Yet 37, or approximately 55 per cent, showed abnormal electroencephalographic findings. In 12 patients who were unconscious for periods of 10 minutes to one hour, abnormal readings were present in six instances, or 50 per cent. Of the 12 cases where unconsciousness persisted for longer than one hour, ten (83 per cent) showed abnormal records. Therefore it would seem reasonable not to place too much emphasis on the absence of unconsciousness in evaluating head injury. Although brain damage is likely to be more severe in cases with more prolonged unconsciousness, the reverse is certainly not true since 50 per cent of patients with minimal loss of consciousness may still show abnormality in their brain wave recordings. As mentioned above,[2–6] the medical literature is replete with evidence that severe brain damage may occur without loss of consciousness, a fact too often overlooked in litigation or compensation proceedings.

A few further clinical correlations might be of interest in these cases. For instance, of 14 patients who showed typically hysterical hemihypalgesia and had therefore been called neurotic, six had abnormal electroencephalographic records. Half of these cases showed focal localization, though in two cases the abnormalities did not correspond with the side of the hysterical symptoms. It is well recognized that functional overflow may be present in association with an underlying organic lesion, but in our experience the latter fact is too frequently overlooked when the functional element is noted. A more accurate interpretation may result from the electroencephalogram in these cases. Lastly, an analysis of findings in relation to duration of symptoms since the head injury occurred was attempted. No correlation could be found, with 29 of 53 cases showing abnormal electroencephalographic findings where symptoms were less than one year in duration, as compared to 24 of 40 cases where symptoms had persisted from one to four years (54 per cent as compared to 60 per cent). These figures certainly do not indicate that prolonged symptoms following minor head injury must necessarily be functional in type. As noted in the previous study mentioned above,[1] where no compensation or litigation factors were present, similar prolonged symptoms were present in about 30 per cent of cases.

SUMMARY AND CONCLUSIONS

1. A series of 95 cases of postconcussion syndrome involved in litigation for compensation were reviewed consecutively. Clinical evaluation has been made of the degree of organic versus functional components in these cases, and a correlation attempted with the aid of electroencephalography in all cases.

2. Definite abnormalities were found in 55 per cent and borderline read-

ings in 3 per cent of this series, despite the absence of positive neurologic findings on examination.

3. The types of abnormalities found are listed, the most common being focal slow waves, although amplitude asymmetries were also of considerable significance. Fast activity was rarely seen.

4. Similar changes were found in recent head injuries of less than three months' duration, as compared with older cases where the head injury had occurred one to two years previously.

5. In approximately 80 per cent of the cases, the clinical impression was confirmed by electroencephalographic findings. In the other 20 per cent the clinical impression was at variance with the records.

6. No correlation could be determined between loss of consciousness and abnormal records.

Even though the head injury had produced no loss of consciousness or only momentary dazing, the same percentage of abnormal electroencephalographic findings was present ($\pm$55 per cent) as in those patients who had been unconscious for periods of ten minutes to one hour.

7. The presence of hysterical hemihypalgesia does not rule out an associated organic brain lesion. Almost half of the 14 patients in this category showed definitely abnormal records.

8. Caution is advised in diagnosing neurosis too casually in patients with postconcussion symptoms persisting for a long while following head injury. An electroencephalographic record should always be obtained and evaluated with the rest of the clinical findings.

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Return of Motor Function in Hemiplegia

Charles Van Buskirk, M.D.

THERE is very little exact information available concerning the return of voluntary motor function in man following hemiplegia. The most recent consideration of this problem by Twitchell[1] outlined a pattern of return of function, presented some observations of value in prognosis, and touched upon the time factors involved. He also presented the pertinent literature appearing prior to 1951 concerned with this disorder. In contrast, there have been numerous contributions regarding the rehabilitation of these patients, a process involving return of voluntary motor function in part, but largely based upon the adjustment of the individual to his disability and the learning of new motor activity. These contributions have included reports of experience with this process[2–13] as well as reports of new technics of rehabilitation.[1,4,13–22]

A topic closely allied to restitution of voluntary motor function in the hemiplegic patient is that of learning of motor activity. Although it is a process used in rehabilitation, it has not been studied in any detail. Following World War I, Franz[23] did consider learning in hemiplegia along with learning in general. The present communication deals with restitution of function in hemiplegia as it is related to the learning of simple motor activity.

Thirty-nine patients from the acute neurology and rehabilitation wards were used in this study. All had some degree of hemiparesis due to upper motor neuron lesions. The etiologies were variable (table 1). Four of the series had bilateral hemiparesis. Ages ranged from 24 years to 76 years, with the largest number in the sixth decade (table 2). Duration of disability varied from ten days to six years (table 3). Thirty of these patients were selected for more complete study. In addition, five normal subjects participated.

Measurements of specific motor activities were obtained, using apparatus which recorded rates of finger tapping, alternate pronation and supination motions of the forearm, and alternate flexion and extension of the elbow (termed alternate motion in this study). In addition, the speed with which a single flexion motion of the elbow could be accomplished (termed speed of motion) was measured. The rates of repetitive movements were expressed

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TABLE 1
CLINICAL ETIOLOGY OF HEMIPARESIS IN 39 PATIENTS

	Number of Patients	
Trauma		2
Multiple sclerosis		1
Vascular lesions		36
Cerebral softenings	24	
Cerebral hemorrhage	7	
Cerebral embolus	2	
Brainstem softening	3	
Total		39

TABLE 2
FREQUENCY DISTRIBUTION OF PATIENTS BY AGE

	Number of Patients
20 to 29 years	3
30 to 39 years	2
40 to 49 years	4
50 to 59 years	20
60 to 69 years	7
70 years or more	3
Total	39

as times per minute and were recorded as the average of three consecutive trials, each lasting one minute. The speed of motion was also recorded as the average of three consecutive trials and was expressed in seconds. Recordings were made daily for five consecutive days of each week and the weekly averages were used to construct performance curves.

All determinations were made with the patient seated and the upper extremity supported by an arm rest which maintained the arm at a 45° angle in relation to the chest wall. Tapping, alternate pronation and supination of the forearm, and speed of flexion at the elbow were all obtained using the same arm rest. With these tests, the arm was secured to the rest by a strap which passed just proximal to the elbow. Tapping was measured using a telegrapher's key which was connected to a timer and counter which registered the number of taps from onset of tapping until one minute had elapsed. Alternate pronation and supination was measured using a metal cylinder lined with sponge rubber into which the hand was inserted. It was necessary to rotate this cylinder through an arc of 120° to activate the counter. The same timer-counter was used as in the tapping test. Speed of flexion of the elbow was measured by an electronic timer activated by two photoelectric cells. In this test the process of flexion interrupted two beams of light, one at the

TABLE 3
DIFFERENTIATION OF BRAINSTEM SYNDROMES

	Number of Patients	
	Selected Series	Total Series
0 to 2 weeks	1	4
2 weeks to 1 month	9	10
1 week to 2 months	7	10
2 weeks to 3 months	4	4
3 weeks to 4 months	1	1
4 weeks to 5 months	1	1
5 months to 1 year	2	2
1 to 2 years	3	3
2 years or more	2	4
Total	30	39

TABLE 4
CLASSIFICATION OF PERFORMANCE CURVES OF THE SELECTED SERIES

	Number of Curves				
	I	*S*	*R*	+	−
Tapping					
Paretic side	20	4	5		
Nonparetic side	19	8	2		
Total	39	12	7	11	18
Supination-pronation					
Paretic side	20	4	3		
Nonparetic side	20	3	4		
Total	40	7	7	18	9
Speed of motion					
Paretic side	20	1	6		
Nonparetic side	18	1	8		
Total	38	2	14	15	12
Alternate motion					
Paretic side	12	14	3		
Nonparetic side	12	13	2		
Total	24	27	5	21	7
Total	141	48	33	65	46

TABLE 5
CLASSIFICATION OF PERFORMANCE CURVES OF NORMALS

	Number of Curves				
	I	*S*	*R*	+	−
Tapping					
Right	5	0	0		
Left	2	2	1		
Total	7	2	1	1	4
Supination-pronation					
Right	3	1	1		
Left	3	1	1		
Total	6	2	2	2	3
Speed of motion					
Right	2	2	1		
Left	2	3	0		
Total	4	5	1	3	2
Alternate motion					
Right	1	3	1		
Left	1	2	2		
Total	2	5	3	3	2
Total	19	14	7	9	11

onset of motion and another on completion of the motion. The time elapsing between interruption of the first and second beams was recorded in seconds. Alternate flexion and extension of the elbow was measured, using a contoured arm rest in which the forearm was placed. This was supported and pivoted at the elbow region. It was necessary to extend and flex the elbow through an arc of 70° in order to activate the recording mechanism. The same timer-counter as used in the tapping and supination-pronation tests was utilized.

The tests were presented to patients by the same person in a uniform sequence of tapping, supination-pronation, speed of flexion, and lastly alternate flexion and extension. Patients were tested in groups and participation was voluntary. The length of time during which individual patients participated in the study depended upon their interest and the length of hospitalization. At times, however, arbitrary limits were set upon the length of time a group of patients was to be tested. All patients were engaged simultaneously in a rehabilitation program which included physical, occupational, and corrective therapy. There was some degree of selection since only those patients who were physically capable of performing the tests could participate. Another factor was the individual's willingness to take part in the program.

Upon examination of resulting performance curves constructed from the weekly averages, it was possible to classify these curves into three special types. There were those which revealed improvement in performance (I), those which revealed little change (S), and those which exhibited diminished per-

formance (R). The results of classification of performance curves for all tests indicate that 141 or 63 per cent exhibited improved performance, 48 or 21 per cent showed little change, and 33 or 14 per cent diminished performance. Both the paretic and nonparetic sides showed an approximately similar incidence of improvement, regression, and little change (table 4). The individual tests all revealed approximately the same ratio of improvement to lack of improvement, with the exception of the alternate motion (alternate flexion and extension of the elbow) test which differed in that the number of improvement curves was less than that of lack of improvement. Very similar data resulted from examination of the performance curves of the normal individuals (table 5).

TABLE 6
CLASSIFICATION OF PERFORMANCE CURVES AS RELATED TO THE PERIOD OF DISABILITY

Period of Disability	*Number of Curves*							
	Paretic Side			*Nonparetic Side*				
	I	*S*	*R*	*I*	*S*	*R*	+	−
½ month	4	0	0	3	1	0	2	2
¾ month	14	1	1	15	1	0	8	8
1 month	13	3	3	13	3	3	7	12
1¼ months	11	1	0	10	2	0	5	7
1½ months	4	0	0	4	0	0	4	4
2 months	4	4	1	4	4	1	9	0
2¼ months	0	3	0	2	1	0	1	2
2½ months	4	4	4	4	4	4	6	2
2¾ months	0	0	0	0	0	0	0	0
3 months or more	20	10	6	18	10	8	25	11

Table 6 presents the performance curves in relation to the length of time that the disability had existed. Among those patients whose disability had been present less than two months the ratio of improvement to lack of improvement is greatly in favor of those exhibiting improvement, while after two months such a condition does not obtain. The data was quite similar for both the paretic and nonparetic extremities.

It has been demonstrated by Franz[23] and others [24,25] that temporal conditions are important in learning, for example, if rest periods are too long between exercise periods, learning will fail to occur and some loss of ability may occur. In the present series there were eight patients who were tested in such a manner that there were rest periods of varying length between testing series. The characteristics of the performance curves following these rest periods are summarized in table 7. It was found that patients whose disability was two months or less in duration tended to show continued improvement during the rest period on the paretic side, while those with a disability of longer duration tended to show no improvement or regression. The nonparetic limb showed a tendency toward lack of improvement following the rest periods no matter how long the disability had been present (figure 1).

TABLE 7

CHARACTERISTICS OF PERFORMANCE CURVES FOLLOWING A REST PERIOD AS RELATED TO THE PERIOD OF DISABILITY

Period of Disability	*Number of Curves*					
	Paretic Side			*Nonparetic Side*		
	I	*S*	*R*	*I*	*S*	*R*
1 month	4	2	0	2	2	2
2 months	8	0	0	0	4	4
10 months	0	0	4	0	2	2
1½ years	2	2	0	0	4	0
5 years	0	2	2	0	4	0
9 years	0	4	0	0	4	0

TABLE 8

CLASSIFICATION OF PERFORMANCE CURVES AS RELATED TO ORGANIC BRAIN DAMAGE

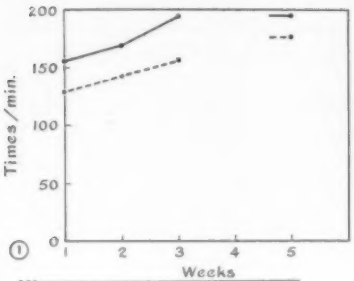
Degree of Damage	*Number of Curves*					
	Paretic Side			*Nonparetic Side*		
	I	*S*	*R*	*I*	*S*	*R*
Marked	8	3	7	6	4	4
Moderate	16	0	0	12	2	0
None	9	2	0	7	1	3

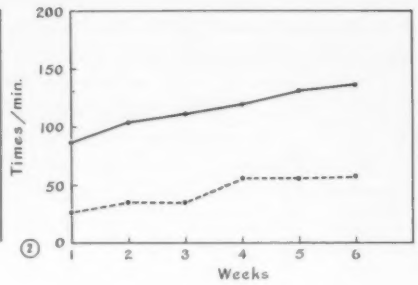
Three patients of the selected series had suffered bilateral hemiplegia. In these, the usual ratio of improvement to lack of improvement had been reversed. This group exhibited six improvement curves as against 11 unchanging curves and seven with lack of improvement. It is to be noted that in this particular small group all patients were in the sixth decade of age but had had their disability well over two months.

Psychometric evaluations of organic brain damage using the Hunt, Bender-Gestalt, and Wechster-Bellevue tests were secured for 12 patients in the selected group. Table 8 presents the performance curve characteristics for this group. Those patients with marked organic deterioration exhibit a reversal in the usual relation of improvement to lack of improvement, while those with a moderate degree of deterioration and those with no evidence of deterioration by the usual psychometric tests revealed the usual predominance of improvement performance curves.

Fourteen of the selected series presented aphasia of various types. All but two of these presented clinical evidence of lesions posterior to the central sulcus. The performance curves of this group preserved the same ratio of improvement to lack of improvement as did the total selected series. Almost all patients in the selected series achieved a satisfactory result in rehabilitation. It is the practice in this hospital to grade rehabilitation achievement in two categories, ambulation and self care. Almost all patients of this series received a perfect rating in both. Four patients failed to obtain a satisfactory rating. One had less than satisfactory ambulation since his nonparetic limb had been amputated. Another left the hospital before reaching maximum hospital benefit, another died, and the fourth exhibited involuntary movements suggesting basal ganglia damage. The achievement in rehabilitation could not be correlated in any way with the performance curves on the motor tests used in this study. It is not surprising that as a group they should do well in rehabilitation since the nature of the tests would eliminate the more severely disabled patients.

The performance levels on the first day of testing ranged from 28 to 391 per second for tapping, 8 to 181 per second for alternate supination-pronation,





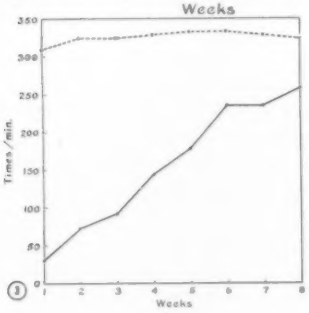


FIG. 1. Performance curve for supination and pronation of the forearm of a 33 year old male with right hemiplegia which had been present for two months. The broken line is the right side and the solid line the left.

FIG. 2. Performance curve for supination and pronation of the forearm of a 49 year old male with a right hemiplegia which had been present for ten months. The broken line is the right side and the solid line the left.

FIG. 3. Performance curve for tapping of a 54 year old male with a left hemiplegia which had been present for one and one-third months. The broken line is the right side and the solid line the left.

0.87 to 0.15 seconds for speed of elbow flexion, and 4 to 108 per second for alternate flexion and extension of the elbow. The best values of the patient series approximated the averages of the normals which ranged from 300 to 392 per second for tapping, 88 to 169 per second for supination-pronation, 0.14 to 0.07 seconds for speed of elbow flexion, and 62 to 214 per second for alternate extension and flexion of the elbow. The initial performance levels could not be correlated with the length of time the disability had been present, the presence or absence of aphasia, the age of the patient, or the handedness of the patient. It could be correlated with the strength of the patient's extremities on admission to the hospital. It was found on referring to the initial examination on entrance to the hospital that the stronger the extremity at that time the better would be the performance on the motor tests of this study.

The initial performance levels for the paretic limbs almost always showed a performance inferior to that of the nonparetic limb. This relationship of performance levels obtained throughout the testing period. Thus, the curves of the paretic and nonparetic extremities were often similar but were at different levels of performance (figure 2). Such similarity was not always the case. In table 4 the number of similarities between opposite limbs is indicated by plus (+) and the dissimilarities are indicated by minus (−). There were 65 similarities as against 46 dissimilarities. It was found that those patients whose disability had been present less than two months had a slightly greater tendency to exhibit lack of similarity between the performance curves of the

paretic and nonparetic extremities. After two months the tendency was toward similarity (table 6). It was determined that one reason for this trend was that although both extremities might show improvement curves in patients whose disability had been present a shorter time, the paretic limb often exhibited more rapid rate of improvement at first so that the performance curves would not match (figure 3).

DISCUSSION

Recovery of function following lesions in the motor system is somewhat similar to learning, and consequently has invited the interest of both psychologists and neurologists. Studies on learning in man are quite extensive, but those on the brain injured man, particularly the hemiplegic, are not. Franz[23] considered re-education in patients with brain injuries a matter of habit formation and discussed methods of measuring movements in such patients. He presented performance curves derived from such measurements. His curves showed gradual improvement for a time followed by a plateau and then regression. The same types of performance curves were evident in this study. He noted that simple tasks were easier to learn and that an incentive must be present for improvement to occur. Franz and others[24,25] have emphasized the necessity of a reward as motivation for learning. Certain other factors are considered essential for learning. Among these are exercise and frequency of practice. All these factors were noted to be active in the present study. Another factor which was undoubtedly operative but which was not evident is that of cross education, first described in the last century.[27] In normal individuals it was found that training of one hand resulted in improved function of the opposite side. Workers during that period also found that such exercise would result in increased strength as well as muscle girth on the opposite side. Several explanations have been advanced for this phenomenon, among them emotional adjustment, training of attention, the presence of identical elements in the tasks, that is, the presence of common head, eye, and trunk movements which are used by both sides of the body.[28–30] More recently it has been suggested that some of the postural reflexes may be active in the process of cross education.[31] It has been demonstrated clearly that in brain injured individuals these postural reflexes are active, as in the associated movements of hemiplegia in which contraction of muscles on one side and head position influence and, even involuntarily, produce contraction of muscles on the opposite side.

There is some information available concerning learning in the brain injured animal. Jacobsen[32–34] demonstrated that lesions of the precentral cortex and postcentral cortex did not impair learning ability in experimental animals. Dexterity was impaired in motor cortex lesions but not learning. Other workers have stimulated the motor cortex without producing conditioning[35] and have paralyzed the motor cortex without preventing conditioning from occurring.[36] Data from the present series is in agreement with experimental work suggesting that the voluntary motor system need not be intact for learning

to occur. The paretic extremity retained the ability to learn as well as the nonparetic extremity, although its dexterity and consequently its performance level might be markedly impaired. Autopsies were generally not possible, so that verification of localization of the lesions was not obtained. Clinical evidence, however, plus observations from one craniotomy suggest that lesions anywhere in the motor pathway do not preclude learning.

A factor which apparently did decrease learning ability, as suggested by this series, is the presence of severe mental deterioration determind by standard psychometric methods. The presence of marked deterioration did not seem to affect the paretic side any differently than the nonparetic side, but seemed rather to depress learning bilaterally. If mental deterioration can be considered a measure of the amount of cerebral tissue which is lost or not functioning, then the same situation is present in bilateral hemiplegia where more brain damage is more likely to exist than in the usual hemiplegia. The three bilateral hemiplegics in this series did exhibit impaired learning ability bilaterally. These observations are in agreement with experimental work by Lashley,[26,37] who has demonstrated that to a certain extent loss of learning ability can be correlated with the degree of brain damage.

What process or processes are involved in the restitution of function following brain damage are not known with certainty. The theories concerning this process have been reviewed by Lashley.[26] These theories include that of Von Monakow which suggests that the recovery which does occur is merely a recovery from depressed function and that no reorganization of nervous processes occurs. Goldstein has denied the concept of true vicarious functioning of undamaged areas and believed that the apparent recovery was rather an adjustment by which the organism managed to get along without the functions which had been lost. Others have accepted the possibility that functions might be taken over by structures not previously concerned with them. Whether such vicarious functioning is a purely spontaneous process or is the result of learning has been argued. These are matters which in the individual patient must remain in the realm of speculation, for seldom is the exact nature of the lesion known. Thus, what part of the recovery is due to recovery of only partially incapacitated neurons and what part is the result of so-called vicarious functioning remains unknown. Data from the present series suggest that this recovery of function may be a spontaneous process and not entirely the result of retraining. It was found that, in patients whose disability had been present for less than two months, there tended to be improvement in performance even though there was lack of practice, while the nonparetic extremity exhibited no improvement or actual regression without practice; thus the nonparetic extremity observed the rules of learning and the paretic extremity did not. It is possible that the paretic extremity had undergone a certain amount of practice outside the testing situation which might affect the performance level. Still, the improvement is out of proportion to what might be expected as compared to the nonparetic extremity. This data would support the suggestion that restitution of function is in part spontaneous. It would

further suggest that this spontaneous aspect of restitution occurs within the first two months after the injury.

Examination of the performance curves reveals that learning during the first two months after the injury is more evident (table 6). Whether the greater proportion of improvement which occurs during this period reflects a process of reorganization of nervous tissue or the presence of a greater degree of motivation during this period cannot be determined with certainty. The fact that the paretic and nonparetic extremities both exhibit more evidence of improvement during this period suggests that it is an expression of greater motivation. However, there were patients who exhibited a more rapid rate of learning on the paretic side within the first two months, which would imply the occurrence of a process of reorganization during this period. Twitchell[1] observed in hemiplegia that willed movement returned and flexion deformity disappeared in the upper extremity from 43 to 60 days following the onset of the illness.

Studies on rehabilitation of hemiplegics have indicated that from 75 per cent to 90 per cent of these patients can learn enough to at least walk and care for their personal needs, and from 49 per cent to 60 per cent are capable of partial or full time employment.[2–13] These experiences have also resulted in a knowledge of the factors which limit the amount of relearning of which a patient is capable. It is a well accepted principle in rehabilitation that for best results such a process should be started immediately after the onset of illness. This study indicates that although learning can occur at any period after the onset of the disability, it is more evident during the first few months, and in addition restitution of function occurs during this period. These factors undoubtedly account for the better results which accrue on instituting rehabilitation at this time. During this period, only encouragement and the simple measures for preventing contractures will frequently produce excellent results. Such measures can easily be instituted in the home and often are. Those patients who enter a rehabilitation program later without doubt constitute the more severely disabled and produce the poorest results. Other factors which limit rehabilitation include mental deterioration. This study indicates that learning of simple motor acts also is reduced when this condition is present. Both the paretic and nonparetic extremities suffer. Since satisfactory rehabilitation depends on the intact upper extremity acquiring an increased degree of dexterity, it cannot be attained in the presence of severe organic deterioration. The mainstay of rehabilitation has been established as motivation. This is the sum of numerous psychologic and physiologic factors which are difficult to measure. The present study did not help to define them.

SUMMARY

The ability to learn simple motor tasks was studied in a series of 39 hemiplegic patients. It was determined that, although dexterity is decreased on the paretic side, the ability to learn remained equal to that of the nonparetic side. Learning on both the paretic and nonparetic sides is more satisfactory during

the first two months after onset of the disability. Where the disability has been present longer, there is less likelihood of learning occurring. Restitution of function following cerebral injury occurs chiefly in the first two months and appears to be a spontaneous process.

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Radioactive Phosphorus in Management of Brain Tumors

Richard W. Garrity, M.D. and LeRoy W. Matthews, M.D.

DURING THE PAST DECADE many diagnostic technics have been developed which facilitate the practice of medicine through the use of radioactive isotopes. Among these are a number directed toward the demonstration and localization of neoplasms of the central nervous system. Many of these technics have not been practical but others have proved quite valuable.

At the present time neurosurgeons have not generally adopted the technic employing radioactive phosphorus with a needle probe counter for brain tumor localization. This diagnostic and localizing aid need not be limited to teaching and research centers, but can be easily incorporated into the everyday practice of neurosurgery.

The technic is simple. The necessary equipment consists of a Selverstone-Waters probe counter, a cable plug assembly, and a sensitive scaler or rate-meter. A preamplifier is necessary with less sensitive scalers or rate-meters. Complete, portable, battery-operated units are also available. After obtaining Atomic Energy Commission approval, P^{32} can be obtained sterile and calibrated from a commercial pharmaceutical manufacturer.

The technic employed consists of intravenous administration of one to two millicuries of radioactive phosphorus 12 to 24 hours before contemplated surgery. Subsequently counts are taken in the suspected area through burr holes or after turning a flap.

The technic was first described in a preliminary report published in 1948 by Selverstone and Solomon[1] and later in more detail by Selverstone, Solomon, and Sweet[2] and by Selverstone, Sweet, and Robinson.[3] Its value as a mapping agent was later demonstrated by Selverstone and White,[4] and its acceptance as a valuable procedure was subsequently reported by Mosley and Jefferson[5] in England.

One of the authors became acquainted with the technic during the original clinical investigations and thereafter applied it to a neurosurgical practice in a large non-university hospital, where the procedure became routine. During a period of two and one-half years it was used constantly whenever any doubt existed as to the nature and location of a possible brain tumor.

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TABLE 1

DATA INDICATING DEPTH AND DIRECTION OF COUNTS

In June 1952 2.0 mc. of P^{32} was given intravenously. Under NO2-02-Pentothal anesthesia, subsequent counts were made in the following areas:

(A) Right hemisphere – cerebellum

(B) Left hemisphere – cerebellum

The following counts were made with a needle-type G-M probe. The lack of a satisfactory ratio difference between the right and left side is apparent.

Count Number	*Areas*	*Depth (cm.)*	*Direction*	*C/M*	*Ratio*
1	A	2	Toward right dentate nucleus	132	1.8
2	A	3		116	1.6
3	A	4		172	2.4
4	A	2	Toward lateral edge of right	98	1.4
5	A	2.5	petrous ridge	120	1.7
6	A	2	Down toward lateral edge	126	1.8
7	A	3	foramen magnum (induration)	178	2.5
8	B	2	Toward left dentate nucleus	236	3.4
9	B	3		86	1.2
10	B	4		108	1.5
11	B	4.5		262	3.7
12	B	2	Toward lateral edge of left petrous ridge	156	2.2
13	B	3	Same (induration)	70	1.0
14	B	4		112	1.6
15	B	2	Toward lateral foramen magnum, left side	106	1.5
16	B	3	Toward lateral foramen magnum, left side (induration)	74	1.1
17	B	3	Toward vermis	254	3.6
18	B	4		178	2.5

Its use was also of definite assistance in patients with jacksonian seizures, accidentally discovered intracerebral calcifications, visual field defects not supported by additional symptoms or signs of an expanding mass, and in neurologic deficits not explained by hypertension, atherosclerosis, hemorrhage, embolism, or any obvious neuromedical disease.

As a result of previous enthusiastic reports and our own experience, the authors have come to depend upon this method. Using P^{32}, the surgeon seldom has any difficulty in locating deeply seated tumor tissue. Members of the family may be given fairly definite information, with subsequent modification according to the pathologic characteristics of the permanent microscopic sections.

The original clinical investigations seemed to indicate that radioactive phosphorus probe counting would be of great benefit. Our experience confirms this. During the period from January 1952 to January 1954, P^{32} was used in 24 of a series of 66 brain tumors. In only one of these cases did the

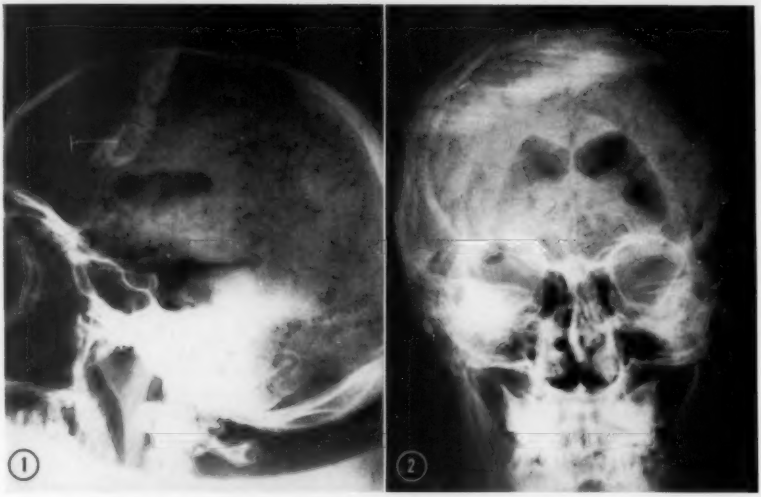

FIG. 1. Calcified area just above normal left frontal horn.

FIG. 2. Posterior-anterior projection indicating no shift or distortion but an absence of right occipital horn filling.

procedure fail to demonstrate the tumor. In this particular patient, a female age 73 with a history of sudden deafness six and nine years previously, the results (table 1) failed to localize bilateral, small acoustic neuromas, 1.5 and 2.5 cm. in diameter, blocking the cisterna ambiens and the tentorial ring. In the remaining 23 cases there was definite verification, localization, and delineation of the tumor mass.

Of the 23 tumors localized and delineated by the probe counter, the ratio between the count obtained in the tumor and that obtained in uninvolved brain varied from 6:1 to 75:1. The higher ratios could not be correlated with the degree of malignancy. Cerebellar astrocytomas frequently demonstrated higher ratios than many of the very malignant glioblastomas.

CASE REPORTS

The following cases are presented to illustrate some of the indications for the use of this method, as well as its diagnostic and surgical value.

Case 1.—A 21 year old man was admitted following the chance discovery of calcification in the left frontal lobe on x-ray films taken after a head injury. There was no previous history of illness or neurologic deficit. Physical examination including careful neurologic examination was normal. The pneumoencephalogram (figure 1) was normal and failed to reveal any involvement of the left frontal horn. Bilateral symmetric frontal burr holes were made and counts were taken in the frontal areas 24 hours after intravenous administration of 2 mc. of P^{32}. Ratios of 12:1 were obtained in the vicinity of the calcifications. Left prefrontal lobectomy carried to the ependymal wall and through grossly normal brain incor-

TABLE 2

DATA INDICATING MARKED CONCENTRATION WITH RESPECT TO OPPOSITE HEMISPHERE AND ALSO WITH RESPECT TO OTHER PARTS OF SAME HEMISPHERE

In December 1953 2.0 mc. of P^{32} was given intravenously. Under general anesthesia, subsequent counts were made in the following areas:

(A) Right hemisphere – cerebellum
(B) Left hemisphere – cerebellum
(C) Midline – cerebellum

The following counts were made with a needle-type G-M probe:

Count Number	*Areas*	*Depth (cm.)*	*Direction*	*C/M*	*Ratio*
1	A	1	Right cerebellar hemisphere–plane	480	6
2	A	2	parallel with midline and 2 cm. lateral	228	3
3	A	3	to midline	100	1
4	A	4		84	1
5	B	1	Left cerebellar hemisphere–in plane	524	6
6	B	2	parallel to midline and 2 cm. lateral	664	8
7	B	3	to midline	2236	27
8	B	4		3364	40
9	B	5		3220	38
10	B	1	Inserted toward internal auditory	516	6
11	B	2	meatis	840	10
12	B	3		444	5
13	C	Surface floor of fourth ventricle		520	6
14	C	1	In midline toward forehead (resistance)	475	6
15	C	2	(More resistance)	388	5

			C/M	*Ratio*	
16	B	Surface of left cerebellum directed up toward petrous ridge	588	1	
17	B	Surface around internal surface of the cavity – 7 cm. x 3½ x 3½	no hot area		
18	B	Surface left hemisphere	492	1	(Different background at completion of operation)
19	B	Surface of cavity	1124	2	

porated an oligodendroglioma approximately 4 cm. in diameter. There has been no evidence of recurrence during a two and one-half year follow-up period.

Case 2.–A 23 year old man was admitted complaining of visual impairment, associated with a seizure preceded by an aura of flashing lights. There were no other complaints and he considered himself to be in excellent health. He was found to have a left homonymous heminopia with macular sparing. Physical, neurologic, radiologic, and electroencephalographic examinations were normal, as was percutaneous angiography. Air study (figure 2) revealed failure of filling of the right occipital horn, which is known to be a common anomaly. Bilateral symmetric burr holes were made and a P^{32} probe counter study performed. A ratio of 7.3:1 was obtained in the suspected occipital lobe. An astrocytoma within the posterior inferior temporal lobe and the right occipital lobe was removed. The patient reports himself to be in excellent health well over two years later.

Case 3.—An 11 year old boy was studied previously in a large teaching hospital. Following a cerebellar exploration the parents were told that no tumor was seen and that the situation was hopeless. On admission to this hospital he presented signs suggestive of a left cerebellar lesion. He was given 1.5 mc. of P^{32} intravenously the day prior to surgery. The following day a flap was turned and counts (table 2) were taken in the cerebellar hemispheres which localized a marked concentration of P^{32} deep in the left hemisphere. Exploration revealed a cystic astrocytoma consisting of a 30 cc. cyst and a 3.5 cm. nodule which was excised. The tumor was found to occupy an area in the left cerebellar hemisphere just beneath the tentorial ring. The patient subsequently recovered completely.

Case 4.—A 35 year old man suddenly developed right hemiparesis with global aphasia. General physical examination was otherwise normal. Neurologic examination suggested the presence of a lesion in the vicinity of the left lower Rolandic fissure. Roentgenograms of the chest revealed a shadow suggestive of neoplasm. Symmetric burr holes were made and probe counter studies carried out, which indicated a "hot" area at a depth of 3 cm. on the left. Punch biopsy in this area was diagnostic for metastatic bronchogenic carcinoma. Necropsy a few days later revealed extensive pulmonary carcinoma with a cerebral metastasis 2.5 cm. in diameter, with hemorrhage in its center and reaction in the surrounding white matter.

A postmortem count of the pulmonary lesion revealed a higher level of radioactivity than the cerebral lesion. It is possible that a diagnostic technic could be worked out for pulmonary malignancies utilizing this tendency of the lesions to concentrate P^{32}.

The following case is presented to demonstrate the value of negative findings.

Case 5.—A 30 year old man had suffered severe head trauma several years previously and presented a history of jacksonian seizures over a period of three years, during which neourologic examinations were normal. The additional history of olfactory aura in 1952 led to a P^{32} probe counter study of both medial temporal lobes through symmetric burr holes. No significant concentration of P^{32} could be localized. Pneumoencephalography was also normal. This patient has been controlled with anticonvulsant drugs and has developed no further signs of tumor during the past two years.

DISCUSSION

In our experience the use of P^{32} probe counting has proved to be of marked value and is used routinely whenever angiography fails to give fairly definite information with respect to the location and nature of the tumor. It is necessary to administer the isotope at least 12 hours in advance, and for this reason angiograms are usually done on the day preceding contemplated surgery. This allows time for ventriculography the morning following inconclusive angiography and at the same time allows for adequate uptake of the isotope in the tumor area.

If a situation arises in which the neurosurgeon must delay surgery, the P^{32} probe counting possibilities are not jeopardized and may be done at any time over a period of several days. This situation is in marked contrast to other external counting methods. We have seen no ill effects in patients without tumors who have received P^{32}.

We have also found scanning of the tumor bed after surgery to be a valuable procedure. On at least one occasion residual tumor was located and removed. A negative scan does not rule out the presence of small nests of tumor tissue but tumor masses larger than 0.5 gm. can usually be localized.

This diagnostic aid can be utilized in any institution where radioisotopes are available. The technic is simple and the equipment necessary is relatively simple and inexpensive. The results are easily interpreted. It is obvious to everyone in the operating theater that tumor tissue is being approached because of the rapidly changing light and/or sound effects from the scaler or rate meter.

SUMMARY

1. Radioactive phosphorus probe counting is a diagnostic aid, now used in a number of teaching centers, which is applicable to the general practice of neurosurgery.

2. It serves as a distinct aid in determining the location and extent of tumor masses and in the early identification of tumor tissues.

3. The method presents a more objective technic for investigating slightly suspicious cases with normal angiography and/or encephalography.

4. The neurosurgeon is no longer placed in the position of suspecting the presence of an expanding mass and being unable to produce pathologic evidence of the tumor.

5. There has been no evidence that this small amount of radioactive phosphorus is in any way injurious to the patient.

6. This method presents none of the disadvantages present in other methods requiring exact timing, tedious studies, or cumbersome and expensive or even unobtainable equipment.

CONCLUSION

The use of P^{32} brain tumor localization technic is a definite diagnostic aid which can be extended to the general practice of neurosurgery.

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CORRECTION

I. C. Sherman and H. M. Seidner: An unusual case of diffuse sclerosis occurring in pregnancy, Neurology 4:637-642, 1954.

The authors regret that the following footnote was inadvertently omitted from the original manuscript. "We are indebted to Dr. J. Luhan of Chicago for his preparation and description of the microscopic material as well as other valuable assistance in the formulation of this article."

Use of Milontin in the Control of Petit Mal Epilepsy

Charles H. Carter, M.D.

TREMENDOUS ADVANCES both in pathogenesis and in treatment have been made in the field of epilepsy during the past few years. Although diagnostic aids such as the wide spread use of the electroencephalograph have aided in the classification of the epilepsies and in more accurate diagnosis of the type present in a given individual, a major field of endeavor has been the search for and evaluation of better therapeutic agents. Although several new agents have been introduced, the major shortcomings have been limited degrees of effectiveness and the development of toxic symptoms after prolonged use. Continued research has brought about the development of several new agents, and one of these is the subject of this report.

Milontin, or N-methyl-α-phenylsuccinimide, has been screened by laboratory tests[1] and found to be most suitable for trial in the petit mal epilepsies. Early clinical studies[2,3] confirmed this impression and the primary emphasis in most studies has been treatment of petit mal epilepsy.

Pure petit mal epilepsy is not seen too frequently and most of the studies so far reported have been with mixed types of epilepsy. In our hospital the patients are of the mixed type. In an attempt to evaluate Milontin a group of these patients were chosen for therapeutic trials.

MATERIALS AND METHODS

The subjects, 81 in number, were all hospitalized patients. As far as practicable the groups were divided equally as to sex. The age range varied from nine to 57 years. Diagnosis was based on clinical criteria and in no case was an electroencephalographic study carried out. Complete hematologic studies were done in all patients prior to institution of therapy, at monthly intervals during therapy, and at three month intervals thereafter. Urinalyses were done on the same schedule as the blood examinations.

All patients were started on an initial dosage of 0.5 gm. daily and increased weekly by 0.5 gm. as required. On the average, control was obtained with 0.5 gm. three times daily. In two patients it was necessary to increase the dosage to 1.0 gm. three times daily. All patients were on combined therapy

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and Milontin was added to the medication already being given. No incompatibilities were observed between Milontin and any of the other anticonvulsants currently employed.

Since the patients were of the mixed type a record was kept of the number of grand mal and petit mal attacks occurring during the period of therapy. Therapy was continued for a ten month period in all cases.

RESULTS

Table 1 lists the results obtained with Milontin therapy for the control and treatment periods. It will be noted that in the male group the number of major seizures increased during the period of therapy, whereas in the female group there was a significant decrease. In both groups there was a very significant decrease in the minor seizures, particularly in the female group. On the basis of these results we can confirm early impressions that Milontin is not particularly effective in grand mal; in certain instances, by controlling the petit mal component, the grand mal component may predominate and an actual increase of major attacks ensues. The degree of control of petit mal attacks is quite similar to that which has been previously reported by various investigators.

TABLE 1

RESULTS IN A SERIES OF 81 EPILEPTIC PATIENTS TREATED WITH MILONTIN

Number of Patients	*Sex*	*Type Seizure*	*Total Seizures* — *Control Period*	*Total Seizures* — *Treatment Period*	*Remarks*
39	F	Major	12,129	10,550	12.7% decrease
	F	Minor	18,096	9,058	49.4% decrease
42	M	Major	13,096	19,938	34.3% increase
	M	Minor	12,184	10,399	14.7% decrease

Other than an occasional episode of drowsiness, there were no untoward side effects. When drowsiness occurred a reduction in dosage with a gradual return to the therapeutic level usually produced no further untoward effect. In one case, however, drowsiness persisted and withdrawal of the drug was necessary.

No changes in the blood or urine were observed during or after the period of medication.

DISCUSSION

Although Milontin does not provide adequate control in all cases, the results obtained are as good as those we have previously observed with other anticonvulsant agents. A particular virtue of this therapy is the freedom from side effects. Although Millichap[3] reported urinary changes in approximately half of a series of patients under treatment, some of whom experienced hematuria, these findings have not been confirmed by others or by us. In a later

paper Millichap[4] reported that similar changes were observed with other drugs currently employed, such as Tridione and Malidone, and thus the significance in relation to Milontin is not definitely established. In view of our findings and those of a large group of individuals who have since employed the drug following its general release, we can state that Milontin does not produce any deleterious effects on the urinary system.

An observation of some interest is that a few patients display alertness, a greater sense of well-being, marked improvement of appetite, and much less abnormal behavior. This finding has been recently confirmed by Forrer.[5]

It is noteworthy that in this series there were no significant changes in the blood and no disturbances in vision, a side effect which has been observed quite frequently with certain of the other anticonvulsant drugs. Forrer[5] has likewise reported on the freedom of toxicity as far as the hemopoietic system was concerned in patients who have received the drug for periods over a year.

Note: In another group treated with Milontin but not included in this report due to the small number of cases, there were nine patients diagnosed as cases of focal psychomotor epilepsies by electroencephalography. Their ages ranged from 12 to 50 years. The average number of convulsions per month for one year before treatment was 90.13 per patient. In the year following treatment the average number of convulsions per month per patient was 10.09. There were no unfavorable reactions to medication and the general well being of the patients was greatly improved.

SUMMARY

1. Milontin has been demonstrated to be an effective drug for the control of petit mal epilepsy.

2. In certain instances of mixed epilepsy, the number of grand mal attacks may be increased with a concomitant decrease in petit mal attacks.

3. No significant changes in the blood or urine were observed following a ten month period of therapy.

4. Because of freedom from toxicity and effectiveness, Milontin is worthy of trial in the treatment of petit mal, either of pure or mixed type.

5. In a very small group of psychomotor epileptics the response to this drug was very good.

Milontin for this study was furnished through the courtesy of the department of clinical investigation, Parke, Davis & Company, Detroit, Michigan.

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CLINICAL PATHOLOGIC CONFERENCE

Raymond D. Adams, M.D.

Section Editor — with the assistance of E. P. Richardson, Jr., M.D.

Presented by Martin G. Netsky, M.D.

CASE PRESENTATION

DR. F. TORRES: A 49 year old white, right-handed waiter was admitted to Montefiore Hospital on August 2, 1950 with a chief complaint of difficulty in walking. Ten months prior to admission he noticed a sudden onset of tightness and numbness of the left side of the forehead. Over a period of five or six months this sensation radiated to the entire forehead, right side of the face, and across the upper lip. Four months prior to admission paresthesias appeared in the right fingers. Three months prior to admission there was weakness of both ankles, which progressed to both knees. As a result of this weakness, the patient could not walk without support. At that time he noticed a tendency to fall to the right. Six weeks prior to admission, he developed blurred vision and intermittent diplopia. He noticed numbness of the tongue, more on the right than on the left, and difficulty in differentiating hot and cold in his mouth. The past history and family history were non-contributory.

On general physical examination, the blood pressure was 140/95; there were no other significant findings.

On neurologic examination, he walked with a wide-based unsteady, hesitant gait, looking at the floor, with a tendency to veer to the right. The left shoulder was held higher than the right. There was a positive Romberg reaction. Adiadokokinesis, increased rebound, and ataxia were found in the right arm, with ataxia in both legs, more pronounced on the right. The deep reflexes were hyperactive on the right side, with right angle clonus, right Babinski, and bilaterally absent abdominals. Sensory modalities were normal. The pupils were unequal in size, but changing; sometimes the left was larger and sometimes it was smaller than the right. There were diminished corneal reflexes bilaterally, slight ptosis of right upper eyelid, upper motor neuron type right facial palsy, and decreased pharyngeal reflex. The uvula deviated to the right.

Laboratory examination revealed fasting blood sugar: 99 mg., blood urea nitrogen: 17 mg. Examination of urine was unremarkable except that porphyrins in the urine were reported positive on August 14, 1950 and August 15, 1950, and negative on February 23, 1951. The complete blood count was normal on admission. The white blood cell count went up to 19,000 on January 21, 1951. A few days later the blood count showed: hemoglobin 13.5 mg.; red cell count 4,630,000; white cell count 10,500 with 82 per cent polymorphonuclear cells and 12 per cent lymphocytes. Serologic tests for syphilis were negative in blood and cerebrospinal fluid. Stool guaiac test was negative. The electrocardiogram was normal. Lumbar punctures showed normal pressure on repeated occasions with protein 88.8 to 102 mg. per cent; sugar 92 to 67 mg. per cent; chlorides 447 to 455 mg. per cent; there were no cells. Chest roentgenograms showed some evidence of inflammatory changes on January 19, 1952 and May 16, 1952. Skull roentgenograms were once reported as showing increased density in the left petrous pyramid and enlarged right carotid canal; these findings were not verified

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later. A pneumoencephalogram showed symmetrically dilated lateral and third ventricles, and increased distance between the posterior clinoids and the floor of the fourth ventricle. A left carotid angiogram was normal. Three successive electroencephalograms showed increasingly diffuse abnormality, mostly slow activity, at the end being more prominent in the left hemisphere. Caloric studies were normal, but there was a bilateral conductive type of hearing loss.

The neurologic symptoms progressed over a period of two years. The ataxia increased and new signs appeared. There were a right sixth nerve palsy, scanning speech, and diminished temperature sensation on the right side. Radiotherapy was given with no significant changes (4932 *r* tumor dose). The left motor fifth and right twelfth nerves became involved. On July 16, 1952 the patient became comatose, his temperature went up to 107°, and he died on July 19, 1952.

DISCUSSION

DR. ALFRED BERL (resident): In discussing this case I would first like to go through the signs and symptoms in an attempt to arrive at some localization of the lesion. The tightness and numbness beginning on the left side of the forehead and progressing down the right side of the face and across the upper lip is most certainly a strange complaint. The tightness and numbness are not explained further, and it cannot be determined whether the patient was describing headache or actual paresthesias. The patient did complain of paresthesias of the fingers of the right hand. Then three months prior to admission he complained of weakness, beginning in the ankles and progressing to both knees. This might be due to generalized weakness or fatigue,—or (since we note he later complained of difficulty in maintaining his balance) he might actually be complaining of ataxia or cerebellar hypotonia. The complaint was sufficiently severe to prevent him from walking. He then noticed a tendency to fall to the right, and again the question of whether this was a symptom of spasticity, weakness, or cerebellar dysfunction is not easily answered. Blurring of vision and intermittent diplopia were noted, but never confirmed on neurologic examination. Numbness of the tongue and difficulty in differentiating hot and cold in his mouth imply fifth nerve involvement.

Physical examination revealed only a mild hypertension of 140/95. Neurologic examination revealed an unsteady, hesitant, and wide-based gait with a tendency to veer to the right. Concerning the Romberg sign, a patient with cerebellar disorder demonstrates a tendency to fall whether the eyes are open or closed. If stance is worse with eyes closed than open, one may assume that the Romberg is positive and that there is position sense loss in addition to the ataxia. The adiadokokinesis, increased rebound, and ataxia of the right upper extremity clearly speak for cerebellar disease, as does the ataxia of the lower extremities, again with more involvement on the right side.

Examinations of the sensory modalities failed to reveal position sense loss, which confirms one's suspicion as to the validity of the positive Romberg sign. The pupils were unequal and changing in size. Sometimes the left was larger than the right and vice versa. This appears to indicate an irritative phenomenon of the midbrain. The history does not reveal, however, how long this state continued. Bilaterally diminished corneal reflexes might mean bilateral fifth nerve lesions. Slight ptosis of the right upper eyelid can speak for third nerve involvement or a Horner's syndrome. The patient did have an upper motor neuron type of right facial palsy and mention is made of involvement of the ninth and tenth cranial nerves with a decreased pharyngeal reflex and deviation of the uvula to the right; in other words, a left glossopharyngeal nerve lesion. Taste is not recorded or was not tested. He complained of difficulty in differentiating hot and cold in his mouth. There is no fur-

ther mention as to whether this was brought out on physical examination. I accept this loss of hot and cold differentiation, despite the fact that there was no objective sensory loss mentioned. I assume that there were no abnormal findings in the fundi. There was no mention of any extraocular muscle palsy at this time, yet the man did complain of intermittent diplopia. Visual field studies are not mentioned so I assume that either they were not done or that they were normal.

In laboratory tests we get the interesting finding that porphyrins were positive in the urine on two occasions one day apart, and negative about six months later. Now, the presence of porphyrins has little meaning, if this is the ethyl-ether fraction rather than the ethyl-acetate fraction. Coproporphyrins picked up in the ethyl-ether fraction are not of concern to us in the intermittent type of porphyria. Coproporphyrins are increased in liver disease, in the lead encephalopathies, in any type of degenerative disease, or in diseases producing cachexia. In the intermittent type of porphyria the porphyrobilinogens are present in the urine even in the stages of remission, and these are pathognomonic, as in the screen test for the porphyrins present in urine. Thus I assume we can rule out porphyrinuria.

We have a few more laboratory findings of interest. The white blood count went up to 19,000 on January 21, 1951. A white count that went up on one occasion and then returned to normal implies an acute infection. Serology was negative. Lumbar puncture showed a normal pressure and protein on repeated occasions. No cells were found in the fluid at this time. Chlorides were low, but I don't think they are of significance. The skull roentgenographic findings of an increased density in the left petrous pyramid and enlarged right carotid canal were not later verified on repeated studies.

DR. TORRES: May I say a word about that? They requested new special roentgenograms and in the new studies they did not find it.

DR. BERL: When they saw the old studies again after the new studies, did they still find the increased thickening?

DR. TORRES: They did not think this was significant because the special studies did not show it.

DR. BERL: The pneumoencephalogram showed symmetrically dilated lateral ventricles and increased distance between the posterior clinoids and the floor of the fourth ventricle. This, I think, is a very important finding in terms of helping us in our differential. The angiogram is normal. If there is a lesion, it is in the posterior fossa and we would not be able to see any involvement of the carotid artery, or the anterior and middle cerebral arteries. Three successive electroencephalograms showed a progressive type of slow wave abnormality, increasingly diffuse. Hearing loss of conductive type was present bilaterally, with normal caloric studies. We don't know how severe the hearing loss was. This is of importance in view of the fact that involvement of the eighth nerves comes up in the differential diagnosis in this patient. The neurologic symptoms did progress for a period of two years, giving a two and a half year history in all. The ataxia increased. He developed a right sixth nerve palsy, scanning speech, and diminished temperature sensation on the right side of his face. Radiotherapy was given with no definitive results. He finally developed a left motor fifth and a right twelfth nerve palsy. Terminally the patient's temperature went to 107°.

I don't think there is any question of the location of this lesion. One has to place it somewhere in the brainstem to accommodate all these signs. Descending and ascending tracts are involved. As to the possible types of lesions, let us first consider a vascular etiology. The

two and a half year history with relatively slow, progressive onset and progressive course does not sound at all like a vascular lesion. Therefore, let us consider degenerative diseases. Multiple sclerosis is a possibility. The course is intermittent at first because of the diplopia. However, while it is true there are many structures involved, I don't think there are disseminated lesions. The areas immediately around the medulla and pons appear to be the only ones affected. We know a localized encephalitis in the brainstem is possible, but again the onset is usually more acute and the patient has more discomfort. This man complained for ten months prior to admission. Of other degenerative diseases, I want to mention in passing Schilder's disease, where, however, there is more cortical involvement, young people are chiefly affected, and the patient has blindness and seizures. If syringobulbia existed by itself symptoms something like this might occur as the lesion is progressing. However, in most cases syringobulbia is an extension of a syringomyelia and atrophy of the tongue is almost always present. The classical triad of syringobulbia is nystagmus, atrophy of the tongue, and a dissociation of sensory findings. Sometimes syringobulbia can exist alone, but when it does it extends down to involve the cord shortly thereafter. At best this is a very unusual site for this type of lesion to begin, and I think it can be discarded from the differential diagnosis.

Finally, we must consider tumor. The pneumoencephalographic findings of the dilated lateral and third ventricles and increased distance between posterior clinoids and the floor of the fourth ventricle point to a lesion of the pons and medulla, either within the pons or medulla or outside of the pons and medulla. There are a few points about these types of lesions. They are unusual, and the finding of an intermittent or a communicating partial hydrocephalus is perfectly consistent with this type of lesion. The patient does not complain of increased intracranial pressure, especially if the condition goes on to involve the pons as cited in various reports of cases. Alpers and Yaskin[1] have described tumors of the pons, and in general they found that headache and increased intracranial pressure, when present, occur late. This lesion does tend to occur in the younger age groups but is found in older individuals. One of the things that might lead one's thoughts outside the brainstem itself to lesions pressing on the brainstem is the diffuse type of lesion that occurs in this case, where findings are on both sides. It is true that in gliomas of the pons and medulla, you may obtain findings of diffuse involvement, yet they are not as diffuse. Some extrapontine lesions that we might be looking for, such as fourth ventricle tumors, give an early increase in intracranial pressure and sudden vertigo with change of position of the head. Cranial nerve involvement does not occur early until there is increased intracranial pressure.

We must now consider an extramedullary lesion. A neurinoma of the eighth nerve can be pretty well ruled out. There are also pearly tumors (cholesteatomas) which are very rare. A chordoma can project into the interpeduncular fossa, or it may project down beneath the pons and midbrain back to the cerebellopontine angle. One may not see increased intracranial pressure in these cases until very late. Compression of the cerebral peduncles gives rise to pyramidal tract signs, and compression of cerebellar peduncles would give cerebellar signs. Another likely possibility is a fifth nerve neurinoma, but in these cases I would expect to see more of a tic douloureux-like picture earlier in the irritative stage of the illness. Here the patient merely complained of a tightness and numbness of the left side of the head and then

across the right, but still that lesion might be considered in view of the fact that it may involve the brachium pontis and then go on to involve the lower cranial nerves. Irritative phenomena of the carotid sympathetics could give the phenomenon of the pupils changing in size in the early stages of the disease. The relative dearth of pyramidal tract signs can also be explained in this fashion. I feel, therefore, that the lesion is extramedullary because of the diffuseness of the signs.

As for making an actual pathologic diagnosis, I feel this is impossible to do. A chordoma, or, because of the sensory or facial nerve disturbance, a fifth nerve neurinoma, are my favored choices. A third possibility is a cerebellar lesion extending down to involve the fifth nerve nuclei, as well as all the other cranial nerve nuclei. The fifth nerve could have been involved relatively early in view of the fact that the cerebellar signs occur at a period almost concomitant with the sensory findings, so far as the history goes. The type of cerebellar lesion extending down must be considered, and here medulloblastoma can be completely ruled out. But a midline astrocytoma or a sarcoma rising from the meninges are two other possibilities.

DR. MARTIN G. NETSKY: What is your final diagnosis?

DR. BERL: An extramedullary lesion, probably a chordoma.

DR. T. J. C. VON STORCH: Dr. Berl, assuming a brainstem lesion, how do you explain the slow activity in the electroencephalogram with the dominance of this slow activity in the left hemisphere?

DR. BERL: I really can't. You can see changes in the electroencephalogram with brainstem disease, but I cannot explain the greater prominence in the left hemisphere. I am not willing to put the lesion there just because of that one finding.

DR. NETSKY: Perhaps Dr. von Storch will bring up that point in his discussion. If there are no further questions, we will ask each one for his diagnosis.

DR. HERBERT I. HOROWITZ (intern): I certainly don't know what this is, but I have some ideas. I think that an inflammatory lesion should be definitely considered. There isn't really enough in the protocol to give us any reason for the elevated white cell count and high polymorphonuclear cell count. Most of the localizing signs seem to be in the midbrain on the left side, yet there are many signs that point elsewhere and the possibility of an indolent inflammatory process certainly is reasonable.

DR. NETSKY: What inflammatory agent would you suspect?

DR. HOROWITZ: In the presence of suggestive roentgenographic lung findings, a case could be made for pulmonary tuberculosis with tuberculoma of the brainstem.

DR. SIDNEY FINK (resident): I also agree that it probably is a brainstem lesion. I would accept the chordoma, but would also consider a glioma of some sort. A benign tumor growing in the area would be most likely.

DR. NETSKY: A glioma would be an intramedullary lesion; a chordoma, we would assume, would be extramedullary. Which would you choose as the strongest possibility?

DR. FINK: They are right in the same area. Between the two I don't think I could tell.

DR. HALSTEAD HOLMAN (resident): I think it's most likely a tumor. I agree with the localization. I don't know about the relative frequency of occurrence of meningiomas in the area and I would like to raise this as a possibility. I suspect more a benign type of tumor because of the duration. The symptoms might be explained by multiple sclerosis, but I feel the findings on the pneumoencephalogram, perhaps the protein, and the fact that the cranial nerve signs all

can be localized to the brainstem would militate against multiple sclerosis in favor of a tumor. I don't know whether it is intramedullary or extramedullary.

DR. GERALD LEVY (resident): I agree with the location. I feel it is a slowly growing neoplasm in that area, probably extramedullary type.

DR. NETSKY: What histologic type would you suspect as your first guess in this case?

DR. LEVY: A chordoma or possibly a meningioma.

DR. MARVIN L. BOBB (resident): For the same reasons which the others have given, I disagree with them. It seems there is some evidence the lesion is on the right, some on the left. Because of the absence of electroencephalographic localization and the fact that the protein is not really very high and that there is no papilledema, I could not be convinced that there is a tumor here and would suspect, because of the age of the patient, possibly there is some degenerative disease such as multiple sclerosis.

DR. KENNETH J. STRULLY (associate attending neurosurgeon): There are several confusing factors in this case. Without the pneumoencephalogram the diagnosis of tumor would be rather difficult to make. However, the picture is extremely suggestive of a neoplasm or a mass lesion. One possibility could be an aneurysm of one of the vessels in the posterior fossa; an eighth nerve tumor could possibly do it, if it extends anterior to the pons; a meningioma, of course, is a good possibility; a Schmincke tumor growing up through the clivus (from the pharynx and through the base of the skull) can produce a similar picture.

An intramedullary tumor would be most likely in this age or any age and could be either an astrocytoma or spongioblastoma polare. Those are the two most common that occur in this area. The picture is not that of an intraventricular or an aqueductal lesion. It is extra-aqueductal and extra-ventricular. It is impossible to state whether it is extramedullary or intramedullary. One of the confusing things to me is the fact that most of the cerebellar signs are on the same side as the pyramidal tract signs. I would expect to have a crossing of signs in that type of thing.

DR. NETSKY: If this were your patient and you thought it was mostly extramedullary, would you be willing to do a craniotomy?

DR. STRULLY: No, I would not. It is an extremely inaccessible area and patients may die spontaneously and very rapidly. I don't feel that a lesion anterior to the medulla or pons is accessible from any approach.

DR. DEWEY K. ZIEGLER: I believe the lesion in this case is in the brainstem, and the early affection of the pharyngeal reflex and of fifth nerve function points to the lower brainstem. The sensory symptoms on both sides of the face suggest that in the lower brainstem ipsilateral fibers in the descending tract of the fifth nerve plus fibers crossing from the contralateral descending fifth tract are both affected, suggesting an intramedullary lesion of the medulla. Impairment of function of the twelfth nerve also is consistent with a medullary lesion.

I would agree with Dr. Berl that the fluctuating pupillary signs indicate involvement of the sympathetic pathways that run in the reticular formation of the brainstem; the other alternative is involvement of the third nerve nuclei in the upper midbrain, which I think is improbable.

Dr. Netsky has emphasized the problem of whether we are dealing with an extramedullary or intramedullary lesion. I would favor an intramedullary lesion for the following reasons: first, the peculiar distribution of disturbance of facial sensation, as noted above, and the marked subjective disturbance of tem-

perature sensation which is often disproportionately affected in intramedullary lesions (e. g. syringomyelia); second, the pupillary instability, probably indicative of a reticular formation disturbance; third, the diffuse electroencephalographic abnormality noted by Dr. von Storch. This abnormality is interesting in view of the work of recent years on the interrelationship of a brainstem reticular formation with basic electroencephalographic rhythms – destruction of this area, for example, producing diffuse slowing.

The elevated cerebrospinal fluid protein is slightly in favor of an extramedullary lesion; the presence of cerebellar and pyramidal tract signs merely support the diagnosis of brainstem lesion and are not helpful in differentiating the intramedullary from the extramedullary. As to the nature of the lesion, chordoma has been mentioned. This is a rare tumor; I believe less than 100 cases have been reported – and there is usually a characteristic x-ray finding in the region of the clivus. The possible extramedullary lesions have been enumerated.

I would favor a pontomedullary glioma. Dr. Strully has mentioned other possibilities as to intramedullary lesions; they are less common.

DR. VON STORCH: I agree essentially with Dr. Ziegler. One of the most interesting things about this case is that it brings out several significant principles of neurologic diagnosis. In the first place, this is the type of case which is commonly diagnosed erroneously as multiple sclerosis, since to the uninitiated there would appear to be signs and symptoms of multiple lesions. In such a situation one must always consider a single lesion in the brainstem.

DR. NETSKY: Are you sure it is an error?

DR. VON STORCH: I am sure it is an error in this case. It is very common to mistake a brainstem lesion for multiple sclerosis, the only reason being a deficient knowledge of neuroanatomy. I think one can say that there is a single lesion here, although it is most irregular in shape. Now the second thing is that this is characteristic of intramedullary brainstem involvement, on the following principle: There is involvement of the long tracts including the autonomic tracts. There is involvement of the reticular substance, and there is involvement of the cerebellar tracts. The only place one can bring those together with cranial nerve involvement is in the brainstem. Now in addition, if you wish to localize further, the lack of increased intracranial pressure and the cranial nerves which were involved indicate to me that the lesion would be confined to the pons and the upper medulla. I believe that the lesion developed from somewhere in the pons near the fifth motor nucleus, spreading caudad to the upper medulla as the disorder progressed. I agree with Dr. Ziegler's comment about the reticular substance and its reflection on the cortical electrical activity, and for that reason I brought the question up earlier.

Now, concerning the etiology, I said this is an intramedullary lesion but intramedullary involvement can be produced by extramedullary lesions. Personally I believe that this is a gliomatous lesion; however, something involving the vascular supply around the pons, such as an aneurysm of the basilar artery involving the vessel in such fashion as to occlude some of the penetrating vessels, would produce a similar intramedullary syndrome. To go back just a moment to porphyria – this is unlikely, but it is to be remembered that porphyria can produce involvement of the central nervous system in any phase, as well as the peripheral nervous system. I don't think encephalitis is a very good diagnosis here. Syringobulbia has been considered unlikely already and I agree with the reasons already given.

I should presume that this is an intramedullary pontine glioma, either a spongioblastoma or even glioblastoma multiforme (some of them are not too rapid in growth) and perhaps even a medulloblastoma, which would be unusual in a patient this age.

DR. NETSKY: In a 49 year old patient?

DR. VON STORCH: I believe a diagnosis of medulloblastoma would be extremely unlikely, so I think that a spongioblastoma or a glioblastoma multiforme of the pons is the best bet. I do not wish, however, to exclude entirely a basilar aneurysm which could cause exactly these findings.

DR. BERL: What about the electroencephalographic findings on the left side?

DR. VON STORCH: I don't know if we have any evidence that reticular stimulation or destruction may cause lateralized cortical dysrhythmias. I do, however, know that the cortex becomes involved, though I don't see why one side would be more involved than the other. The lesion is intramedullary because it affects the long tracts, that is, the cerebellar tracts, the ascending sensory and descending motor tracts, and the cranial nerves. There is no doubt about that. Extramedullary compression, however, might well cause such intramedullary involvement. Hence one has also to consider a meningioma, an aneurysm, and various other things. I am sorry I cannot say more than that I feel that it is intramedullary. However, don't forget aneurysm because an aneurysm or a gradual occlusion of a major vessel could do the same thing.

DR. STRULLY: The pneumoencephalogram is strongly suggestive of intermittent or partial occlusion of the aqueduct. The posterior displacement of the floor of the fourth ventricle indicates a mass anterior to it.

DR. VON STORCH: Oh, I mentioned nothing about that. The pneumoencephalogram as such is conclusive evidence of an intramedullary lesion.

DR. NETSKY: Why is it conclusive?

DR. VON STORCH: Its description is conclusive, that is, no mass was demonstrated outside.

DR. NETSKY: Do you think you could visualize a separate mass if it were closely adherent to the surface of the brainstem?

DR. VON STORCH: If a tumor is just pushing the floor of the fourth ventricle backwards it could be extramedullarly or intramedullary. If you saw that the depth of the pons was actually increased in width, however, one would expect the tumor to be intramedullary.

DR. STRULLY: You have to have a small amount of air in the cisterna pontis to outline a mass anterior to the pons, or to outline the anterior surface of that structure, in order to be able to demonstrate an extramedullary lesion. However, most lesions when they occur in that location, anterior to the pons, fill the cisterna pontis and prevent the air from filling that space. This obliterates any line of demarcation between the two. Swelling of the pons due to an intramedullary mass also fills the space. Therefore, it is almost impossible to determine in many of these instances whether the mass is intramedullary or extramedullary. The important thing is where the lesion lies, whether it is anterior or posterior or lateral to the aqueduct or the fourth ventricle. If it lies anterior, whether it is in the brainstem or out of the brainstem is unimportant, because from the surgical standpoint it is inoperable.

DR. VON STORCH: There is one other point we should consider, that is, the absence of rapidly increasing intracranial pressure somewhat suggests an external lesion which has not implicated and occluded the aqueduct.

DR. STRULLY: I don't think there is any real evidence of rapidly increasing intracranial pressure. The brainstem glio-

TABLE 1

DIFFERENTIATION OF BRAINSTEM SYNDROMES

Extramedullary	*Intramedullary*
1. More often unilateral.	1. More often bilateral.
2. Usual onset with signs of unilateral cranial nerve irritation (tinnitus, pain in face, etc.).	2. Onset varies, depending on location of lesion. Dorsal lesion may involve medial lemniscus, then spread to pyramidal tract, then laterally to spinothalamic tract.
3. Involvement of a group of cranial nerves on one side speaks for extramedullary lesion. Later, compression may produce pyramidal or cerebellar signs.	3. "Crossed" syndromes: alternating hemiplegia (ipsilateral cranial nerve signs with contralateral hemiplegia); or crossed anesthesia (face on one side, body on other).
4. Combinations of fifth and eighth nerve involvement (angle syndrome); seventh and eighth nerves.	4. Sixth and seventh nerve involvement.
5. Ipsilateral external rectus palsy and infranuclear palsies.	5. Early paralysis of lateral gaze (parabducens nucleus); conjugate gaze palsies; loss of convergence, ophthalmoplegia internuclearis anterior.
6. Peripheral third nerve paralysis; all muscles affected almost equally.	6. Nuclear third nerve-orbicularis oculi is affected; single muscle function may be altered.
7. Lateral nystagmus is not helpful.	7. Rotatory nystagmus (vertical nystagmus?).
8. Symptoms of increased intracranial pressure earlier.	8. Pressure symptoms late, unless ventricles are blocked.
9. Complete nerve deafness is a peripheral sign.	9. Nerve deafness rare.
10. Sensory loss usually affects all modalities.	10. Dissociated sensory losses.
11. Concordant vestibular reaction (no response from horizontal or vertical canals); equal nystagmus, nausea, and past-pointing.	11. Dissociated vestibular reactions (vertical canal fibers are higher in pons); dissociation between nystagmus, nausea and past-pointing.
12. Common types:	12. Common types:
Perineurial fibroblastoma (usually acoustic)	Vascular accidents
Meningiomas	Multiple sclerosis
Aneurysms	Gliomas
Extension of cerebellar neoplasms	Bulbar palsy—A.L.S., poliomyelitis
Basal carcinoma or sarcoma, lympho-epithelioma, chordoma	Syringobulbia.
Chronic basal meningitis	

mas often do not cause occlusion of the aqueduct. They cause death by destruction of vital structures rather than by internal hydrocephalus with increased intracranial pressure. This cannot be considered a differential point between extrapontine or intrapontine tumors.

DR. ZIEGLER: In the absence of this ability to determine absolutely whether the lesion is intramedullary or extramedullary, and the possibility that a meningioma or fifth nerve neuroma was present, it would seem to me that probably these patients should be explored.

DR. NETSKY: I am glad that you made that suggestion, because what I have to show may help convince all of you that Dr. Ziegler's statement is correct. There were no abnormalities of the dura or cerebral leptomeninges, the brain was not swollen, and the blood vessels were unremarkable. The principal lesion was a cystic mass, 4 cm. in diameter, which almost completely replaced the left side of the pons (figure 1). The basilar artery was displaced to the right. The photograph shows a small white plaque of dura adherent to the mass. A close-up of the brainstem (figure 2) shows this fluctuant lesion in greater detail. The fifth cranial nerve is not identified and apparently is replaced by the tumor. The sixth, seventh, and eighth cranial nerves are not implicated. In the next picture (figure 3), a cut has been made through the pons and the two facing sections are shown. There is a laterally placed mural nodule. The cyst contains about 8 cc. of a thick, yellow material. The fourth ventricle is compressed by the cyst, resulting in a moderate hydrocephalus. There is only a thin rim of pontine tissue which is seen on the right.

Microscopic examination of the mural

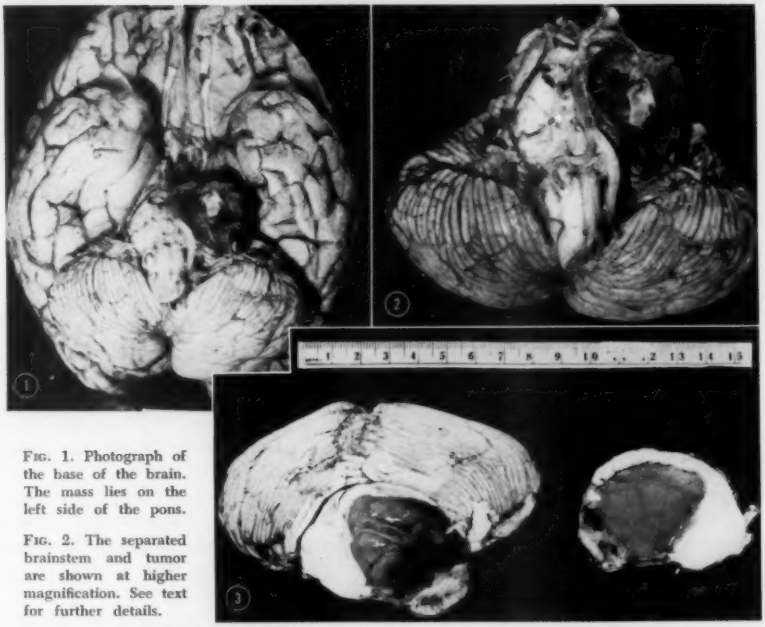

FIG. 1. Photograph of the base of the brain. The mass lies on the left side of the pons.

FIG. 2. The separated brainstem and tumor are shown at higher magnification. See text for further details.

FIG. 3. A cut has been made through the pons and the center of the neurinoma. A mural nodule is present and a large cyst with viscous fluid has replaced most of the pons.

nodule reveals typical fibroblastic formations, palisades, and loose reticular tissue. The diagnosis is: perineural fibroblastoma of fifth cranial nerve (fifth neurinoma).

DR. STRULLY: The lesion would explain the presence of air in the cisterna pontis as seen in the pneumoencephalogram. The lateral placement of the mass allowed a small amount of air to lie anterior to the pons giving the appearance of a normal cisterna. This with posterior displacement of the floor of the fourth ventricle is indicative of an intramedullary lesion. Tomography would have been of great value here, since cuts to either side of the midline would have revealed the absence of air in the left lateral extremity of the cisterna pontis.

DR. NETSKY: I believe almost everyone localized the process to its approximate place in the brainstem. There was uncertainty about the crucial problem of whether this was intramedullary or extramedullary. I have listed in table 1 what I believe are the important differential points. None of these individually will make the diagnosis, but they offer an approach and some aid in this difficult problem. It is always well to recall the point made by Dr. von Storch, that an extramedullary lesion can compress the brainstem and produce effects similar to that of an intramedullary lesion. In this particular case, admittedly using hindsight, I would remind you how important the initial signs and symptoms may be in diagnosis. The earliest complaint was of numbness on the left side of the forehead which went on to in-

volvement of the lid, and to me this was the best indication of the ultimate diagnosis.

In addition, I would like to comment on the error of using radiation therapy on an unknown lesion. In principle, it is bad practice to irradiate a patient whose histologic diagnosis is not known. It is a blind procedure; the sensitivity of the suspected lesion is not known; once radiation is started, the patient is condemned as inoperable; if the opinion should be changed, operative intervention is made more difficult, and time is lost; and finally, the brainstem may be damaged by the therapy. In this particular case, I do not believe radiation was of any value. The lesion found at autopsy might have been removed at craniotomy. I would remind you of a report from the Mayo Clinic by Baker and Bailey[2] of a patient who had a similar history. Ultimately a total removal of a neurinoma was accomplished by a transtentorial approach, and the patient returned to his occupation as a carpenter.

DR. ZIEGLER: Sir Geoffrey Jefferson[3] reported recently on a series of these fifth nerve neurinomas and pointed out the extreme difficulty in diagnosis. The characteristic clinical syndrome was a combination of signs resulting from compression of structures in both the middle fossa and posterior fossa. He noted that the tumor was rarely diagnosed during life and even more rarely operated on successfully.

DR. NETSKY: The patient described at the Mayo Clinic survived. A very important point, as this case illustrates, is that not every one of these patients has a hopeless prognosis. In the vast majority of cases with such a picture, we could do nothing, but an important function of a specialized hospital is to salvage the one case in a hundred.

DR. ZIEGLER: Yes; don't you think the moral of this is that in brainstem lesions nobody is infallible enough to assume that there is an inoperable lesion because there are the rare and atypical clinical cases?

DR. NETSKY: Yes.

DR. STRULLY: You come down to the assumption then that we should always explore?

DR. ZIEGLER: No, only with progressive lesions in which there remains uncertainty of location within the posterior fossa.

DR. STRULLY: Well, all the gliomas of the brainstem are progressive, and any tumor of this type is progressive.

DR. NETSKY: The problem we have before us is to decide what could we have looked for in this patient as we review him now with all our knowledge of the case. As I have indicated, the most suggestive thing to me is the initial symptom. We ought to check a large series of gliomas of the brainstem to see if any started that way. I don't recall any that did.

DR. TORRES: I seem to remember that in the cases of Dr. Jefferson, he pointed out that he saw more often paresthesias than objective sensory changes.

DR. ZIEGLER: That is right; he said he never saw an actual anesthesia.

DR. STRULLY: And yet here you have a fifth nerve which you could not find at all.

DR. NETSKY: Yes, it could not be identified.

I think the majority of these tumors, although small in number, start with paresthesias. I know that Foster Kennedy used to stress the point that the initial symptoms of a fifth nerve neurinoma frequently are paresthetic phenomena in the face, and this should arouse our suspicion when other signs of a mass lesion become apparent. If there is any lesson to be drawn from it I would think that would be the most important one. I don't believe it is infallible but it certainly has to be taken into account.

DR. HOROWITZ: How do you account for the paresthesias being bilateral so early in the course?

DR. NETSKY: Such a tumor can always distort and compress. We may have contrecoup phenomena. I have no other way to explain it.

DR. VON STORCH: In that respect, in retrospect, there is another point against an intramedullary lesion, that is, involvement of the intramedullary sensory descending tract on one side and then involvement on the other side with no involvement in between.

DR. HOLMAN: What was the patient's diagnosis during these two years?

DR. NETSKY: An intramedullary glioma, considered inoperable—hence the decision to use radiotherapy.

DR. STRULLY: I think had we suspected it earlier, about two years before, we might have attacked the tumor by a supratentorial approach. The usual posterior fossa approach to this tumor would have been impossible.

DR. NETSKY: The Mayo approach was a lateral one.

DR. STRULLY: You have to cut the tentorial leaf and go down to the tumor from above.

DR. ZIEGLER: I don't see, though, how bilateral fifth nerve involvement would be in favor of its being an extramedullary lesion.

DR. VON STORCH: Without intervening signs, you see. At the very beginning if we just take the initial symptoms: first, the numbness was in the left forehead, then it was in the right forehead, at which time nothing else is happening.

DR. ZIEGLER: Except that the fifth nerve tract crosses all through the medulla so that you do get crossing fibers.

DR. VON STORCH: Dr. Ziegler is right about that, too, because the fibers do cross.

DR. ZIEGLER: That is why when you get a posterior inferior cerebellar artery occlusion both sides of the face can be affected.

DR. VON STORCH: Dr. Ziegler is right about that.

DR. NETSKY: Some portions of the ascending trigeminal pathway decussate in the medulla, but there are two other tracts with higher but uncertain decussations. There may even be some uncrossed fibers.

DR. STRULLY: On which side was the ptosis? On the right side, was it not?

DR. VON STORCH: The ptosis was in the right eye.

DR. STRULLY: That doesn't go too well with an intramedullary involvement of the sympathetic supply. I would expect, if anything, the left eye would have been ptosed, at least considering the picture as presented here with the section of the brainstem.

DR. VON STORCH: That brings up the fourth and last principle, that is that one can't absolutely be definite as to whether a lesion is intramedullary or extramedullary. It was obviously an intramedullary involvement but what was causing it, an intramedullary or extramedullary lesion?

DR. HOLMAN: It is not of any value to report or talk about porphyrins when you say: "Porphyrins are present." The type of porphyrins present must be identified before there is any significance to the finding.

DR. VON STORCH: In this case it was a red herring. I suspect Dr. Torres inserted that just to see whether we knew that point.

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Neurology BOOK REVIEWS

Connections of the Frontal Cortex of the Monkey

Wendell J. S. Krieg, Ph.D. 1954. Springfield, Illinois: Charles C Thomas, Publisher. 320 pages, 186 illustrations. $10.50.

THIS beautifully printed monograph, illustrated by the author, presents the routes of degenerating medullated nerve fibers which followed minute lesions confined to the cortical layers of the frontal lobe of the monkey. The lesions were made by the method of coagulation first exploited by Dusser de Barenne. The subsequent degeneration of myelin sheaths was traced by the Marchi technic. The larger cortical areas, initially determined for this part of cortex of Macaca mulatta by Brodmann, was subdivided by Krieg into many subareas. These subareas were characterized by minute differences in cytoarchitecture and in the sites of termination of degenerating myelin sheaths.

The author does not attempt to relate the limits of these subareas, which he so determined, with those already outlined for the cerebral cortex of the monkey by other investigators, such as Von Bonin and Bailey (1947). (It would have been difficult). Further, Dr. Krieg has used his own nomenclature for the thalamic nuclei to which the injured nerve fibers projected. Consequently, a thorough understanding of the results of this study requires, 1) that a new cortical map of Krieg's areas and subareas of the frontal lobe be drawn by the reader and compared with those of previous authors, and 2) that Krieg's thalamus be homologized with that of Walker.

Dr. Krieg has an absolute and unshaken faith in the ability of his Marchi method to blacken the myelin of every degenerating nerve fiber, in spite of the fact that his method fails to show degenerations which other investigators have described. It is difficult for this reviewer to believe that the cortex of the frontal lobe in the monkey sends no efferent fibers to the corpus striatum, the hypothalamus, the substantia nigra, the subthalamus, and the pons nuclei (after area 4 injury), or to accept as fact that the ipsilateral corticospinal tract is confined to the ventral funiculus, or that degenerating myelin (after area 4 lesions) is never seen among the nerve cells within the ventral horn of the spinal cord.

This monograph is a careful, painstaking, time-consuming study of the fiber connections of the frontal cortex of the monkey. Experimental neurologists must be familiar with the contents of this volume for these results are provocative and will, therefore, stimulate new investigation. Many years will pass, however, before anyone will have the patience to repeat the whole of the laborious work which preceded the printing of this monograph.

MARION HINES,
Professor of Anatomy,
Emory University Medical School

NEWSLETTER

DECEMBER, 1954

Howard D. Fabing, President
Walter O. Klingman, President-Elect
Francis M. Forster, Vice-President
Alexander T. Ross, Secretary
Dave B. Ruskin, Treasurer

AMERICAN ACADEMY OF NEUROLOGY

Epilepsy Legislation Committee to Hold Special Luncheon Howard D. Fabing, president of the American Academy of Neurology, announces that the special legislation committee of the American League Against Epilepsy will be given a luncheon at the annual meeting of the League at the Ambassador Hotel, Park Avenue at 51st Street, New York City, on December 9. Plans also call for a press conference at 11:00 a.m., preceding luncheon. At this conference members of the committee will discuss with the press its findings and recommendations under the heading: "Equity for Epileptics: A Blueprint for Reform of State Laws Affecting Epileptic Patients."

UCP Presents Awards at Annual Convention At its annual convention in the Mayflower Hotel, Washington, D. C. (November 19-21), United Cerebral Palsy presented awards for distinguished service on behalf of America's cerebral palsied children and adults to Congressman John E. Fogarty of Rhode Island, Senator Edward J. Thye of Minnesota, Chief Justice of the Supreme Court Earl Warren, and Dr. Leonard A. Scheele, Surgeon General of the Public Health Service. Dr. Scheele was also the guest speaker at a special luncheon on Saturday.... As part of the convention, a scientific session was held at the National Institutes of Health in Bethesda, Friday, November 19. Among participants in the program were: Glidden L. Brooks, medical director of UCP; Sidney Farber, professor of pathology, Harvard Medical School; Joseph F. Fazekas, chief of staff, D. C. General Hospital; Evelyn Anderson, National Institute of Arthritis and Metabolic Diseases; and George W. Corner, Jr., assistant professor of obstetrics, Johns Hopkins University School of Medicine. The sessions ended with a presentation of the intramural research program of the National Institute of Neurological Diseases and Blindness as it relates to cerebral palsy.

Neuropathologists Discuss Problems in Cerebral Palsy At the Nassau Tavern on the Princeton University campus, a group of distinguished neuropathologists met (November 11-12) to discuss the present status of research in neuropathology as it concerns the problem of cerebral palsy. The 1½ day meeting was sponsored by the United Cerebral Palsy Associa-

tion in cooperation with the National Institute of Neurological Diseases and Blindness. Subjects under discussion were the correlation of clinical and pathologic data in cerebral palsy; relationship of neuropathology to general pathology as it affects research in cerebral palsy; the problem of recruitment and training of research personnel in neuropathology; and suggested areas of emphasis in the field of neuropathology for the United Cerebral Palsy research program.

Muscle Symposium Held in New York Under the sponsorship of the Muscular Dystrophy Associations of America, a symposium was held recently at the Hotel New Yorker to discuss current advances in basic muscle chemistry, physiology, and pharmacology. Emphasis was placed on biophysical and biochemical methodologies as applied to muscle research. Among the many highlights of a highly informative program was a discussion of recent advances in the use of the electron microscope, with particular reference to cytoplasmic reticulum and mitochondria by H. S. Bennett (University of Washington School of Medicine), and J. W. Harman (University of Wisconsin Medical School); and a presentation of the use of muscle models by W.F.H.M. Mommaerts (Western Reserve University School of Medicine), and others.... This was the third medical conference sponsored by MDAA. The welcoming address was delivered by A. T. Milhorat, chairman of the medical advisory board, MDAA.

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ANA Announces Committee Appointments H. Houston Merritt, secretary of the ANA, announces that past president Roland P. Mackay has appointed as members of the committee for the Sixth International Neurological Congress, to be held in Brussels in 1957, Henry A. Riley, chairman; Pearce Bailey, Paul C. Bucy, Horace W. Magoun, H. Houston Merritt, and A. Earl Walker.... ANA President Percival Bailey has appointed a committee on chronic neurological diseases, with Pearce Bailey as chairman, together with Hans H. Reese and Tracy J. Putnam.

New Appointments at NINDB Dr. Henry A. Imus, formerly head of the physiological psychology branch, Office of Naval Research, has been appointed assistant to the director of the National Institute of Neurological Diseases and Blindness. Formerly a research fellow at Dartmouth Eye Institute, Dr. Imus is known for his work on aniseikonia, motor anomalies, binocular vision, and space perception. During World War II, he developed testing procedures for the selection of stereoscopic range-finder operators in military operations. Since 1946 he has organized a comprehensive extramural research program in sensory physiology and psychology for the Office of Naval Research....

Replacing Dr. Frederick L. Stone as chief of the institute's extramural programs (see November 1954 Newsletter) is Dr. Edward P. Offutt, Jr., a specialist in parasitology. Dr. Offutt has had a distinguished career in the bacteriology department of the University of Rochester School of Medicine, until he joined the division of research grants of the National Institutes of Health in 1950, where he has served as secretary of the microbiology and immunology study section and as assistant chief of the fellowship branch.

Neurological Surgeons Meet in New York The Congress of Neurological Surgeons held its annual meeting at the Waldorf-Astoria Hotel in New York (Nov. 4-6). An important segment of the program was the symposium on cervical trauma in which Edward M. Winant of New York presented the orthopedic aspects; Frank H. Mayfield of Cincinnati, the neurosurgical aspects; Howard A. Rusk of New York, the rehabilitation aspects; and Mr. W. Scott Allen of Liberty-Mutual Insurance Company, the medicolegal and compensation aspects. Also on the program was a panel symposium on the medicolegal aspects of head injury with A. Earl Walker acting as moderator.

Electromyographers Elect New Officers At the first annual scientific session in Washington, D. C. (Sept. 5), the newly formed American Association of Electromyography and Electrodiagnosis elected James G. Golseth, president; Y. T. Oester, president-elect; Paul A. Shea, first vice-president; A. A. Marinacci, second vice-president; Arthur Rodriquez, secretary-treasurer; and Gerald Hirschberg, historian. ... The association is considering a bibliography of all American publications of EMG. The 1955 annual meeting is tentatively scheduled to be in Detroit.

American Academy for Cerebral Palsy Meets in Williamsburg The American Academy for Cerebral Palsy held its 8th annual meeting at the Williamsburg Lodge and Inn, Williamsburg, Va., (November 4-6). Meyer Perlstein, president of the Academy, delivered an address on "The Cerebral Palsy Problem in 1954" and the scientific session included presentations on oculomotor defects; speech and hearing evaluation; aphasia; treatment of the spastic hemiplegic and athetoid quadriplegic; sensory disturbances; and the surgical relief of athetosis and other hyperkinesias.

Forster Reports on 1955 Program Francis M. Forster, program chairman for the 1955 AAN annual meeting, Houston, Texas, (April 25-30), reports that requests for space on the scientific program already are being received. Special atten-

tion is being given to original presentations and to papers on the development of therapeutic modalities in the field of neurology. The unusual clinical syndrome session, which was so successful last year, will be repeated. In addition, Augustus S. Rose is planning a symposium on the research aspects of vascular diseases of the nervous system.... Titles and 200 word abstracts of papers for the program must be submitted not later than January 15, 1955, preferably by January 1st. All communications should be addressed to Dr. Francis M. Forster, program chairman, Georgetown University Medical School, 3800 Reservoir Road, N. W. Washington 7, D. C.

Here and There Percival Bailey, president of the American Neurological Association and professor of neurology and neurological surgery at the University of Illinois college of Medicine, delivered the 1954 Charles A. Elsberg lecture (November 16) in the New York Academy of Medicine. The subject was "Psychomotor Epilepsy - Its Relation to the Visceral Brain." Preceding the lecture, Dr. Bailey was honored at a dinner in the President's Gallery of the Academy.... On October 8, Peter G. Denker served as chairman of a symposium on "Nervous Tension" conducted by the New York Academy of Medicine in its recent public health program.... Lewis P. Rowland has joined the neurologic staff of Dr. Tiffany Lawyer, Jr., at Montefiore Hospital in New York.... Theodore J. C. von Storch has settled in Miami, Florida. ... Benjamin Boshes and Oscar Sugar have been elected president and secretary, respectively, of the Chicago Neurological Society.... Jolyon S. Tucker has moved to Birmingham, Alabama, to be associated with Samuel C. Little.... The neurologic scene has been saddened by the death (September 10) of Dr. Charles A. McKendree, formerly of the College of Physicians and Surgeons and attending neurologist in the New York Institute and the Vanderbilt Clinic....

Percival Bailey

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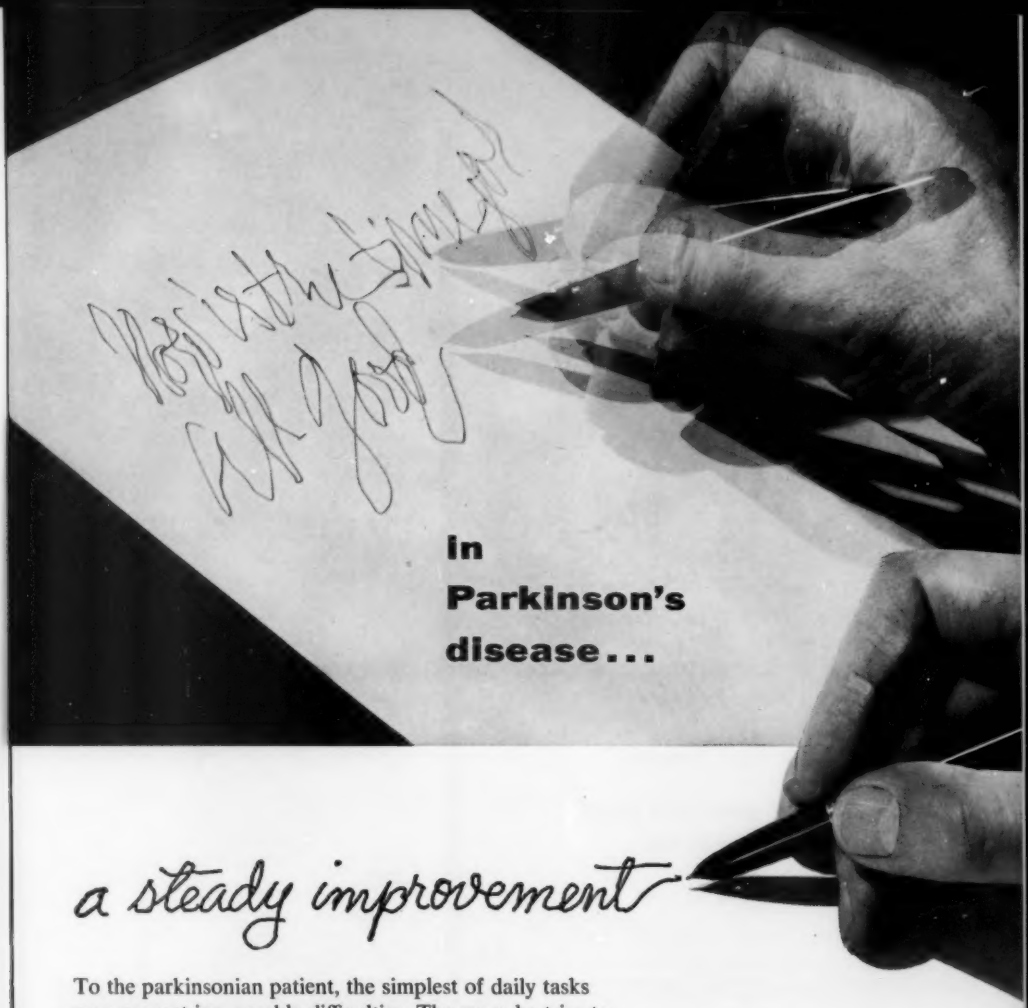

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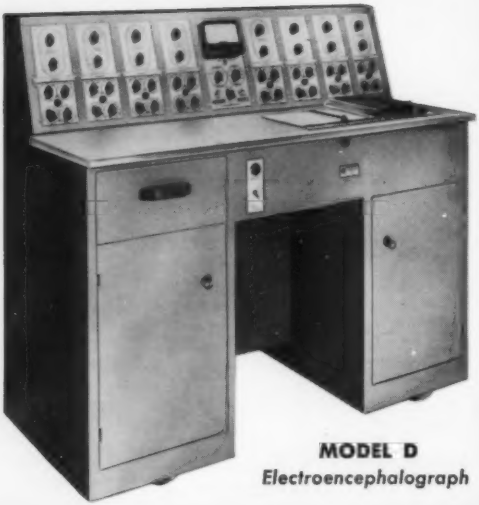

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PUROMYCIN EFFECTIVE IN EXPERIMENTAL AMEBIASIS AND BREAST CANCER

Puromycin, an antibiotic developed at Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York, may turn out to be a valuable new medical weapon, according to reports made to the antibiotics division of the Food and Drug Administration. The drug is not yet on the market.

Puromycin is effective against amebiasis experimentally induced in guinea pigs, according to studies made by D. Jane Taylor, Howard W. Bond, and John F. Sherman under the sponsorship of the National Institutes of Health at Bethesda, Md. In hopes of finding a better drug than those now available, these investigators tried 32 compounds structurally similar to Puromycin. Their tests on mice, rats, guinea pigs, rabbits, cats and dogs have established many of the characteristics of Puromycin.

Puromycin also slows the growth of one kind of breast cancer transplanted into mice. Drs. P. L. Bennett, S. L. Halliday, J. J. Oleson, and J. H. Williams of Lederle have traced the cancer arresting activity of Puromycin to one part of the molecule and have found compounds similar to Puromycin which have the same effect.

MYSOLINE FOR ANTIEPILEPTIC THERAPY

Providing effective antiepileptic therapy with a relatively wide margin of safety, Mysoline, a new anticonvulsant found particularly valuable in the control of grand mal and psychomotor seizures, has been an item of the Ayerst Laboratories, New York, line for six months. Extensive clinical trials confirmed the value of Mysoline employed alone or in combination with other standard anticonvulsants. No serious toxic reactions were reported from its use. Side effects such as drowsiness, ataxia, vertigo, and so on are usually minor and transitory, frequently occurring after initial administration but tending to disappear as therapy is continued or dosage is adjusted.

(Continued on page 16a)

In Main House, at Hall-Brooke, are the administrative offices, the psychiatrist's private offices, the treatment units. Here, also, are the closed halls for men and women patients in this modern psychiatric hospital devoted to active treatment, analytically-oriented psychotherapy, and the various somatic therapies.

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ABBOTT PRESIDENT HONORED

Dr. Ernest H. Volwiler, president and general manager of Abbott Laboratories, North Chicago, Illinois, has been named to receive the Industrial Research Institute Medal for 1955. The medal has been awarded annually since 1945 to honor "outstanding accomplishment in leadership in or management of industrial research which contributes broadly to the development of industry or the public welfare."

Dr. Volwiler's entire business career has been with Abbott Laboratories. Starting as a research chemist in 1918, he advanced through the positions of chief chemist, director of research, and vice-president to the position of president and general manager. During this period, the research organization at Abbott Laboratories developed under his leadership from a group of five people to a scientific division comprised of several departments employing approximately 445 people. Dr. Volwiler pioneered in the field of synthetic pharmaceuticals, was one of the first to develop interest in antibiotic production and research, and encouraged research and development in radioisotopes. His achievement of a high degree of integration of research with the affairs of his company has been outstanding.

TOPICAL ANTIBIOTIC PREPARATION

Hydroderm, a dermatologic antibiotic preparation for topical application, has been introduced by Sharp and Dohme, Division of Merck & Co., Inc.

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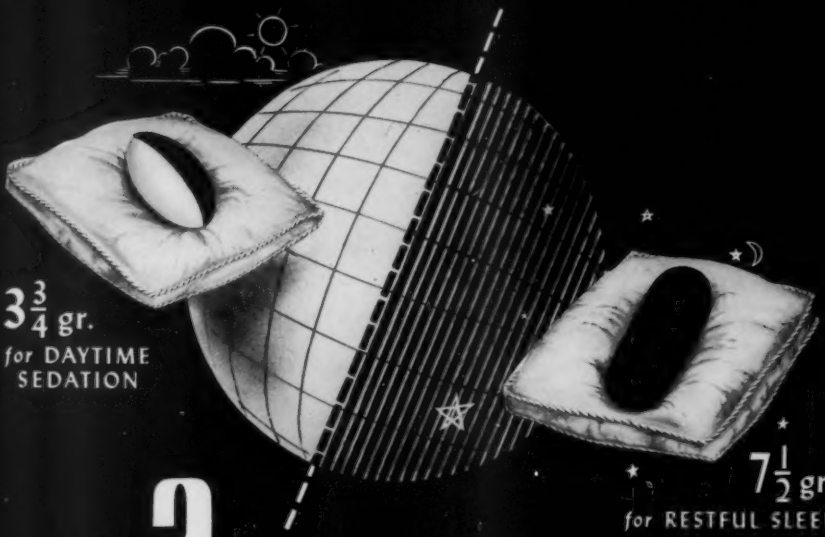

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